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A Weekly Journal of Science

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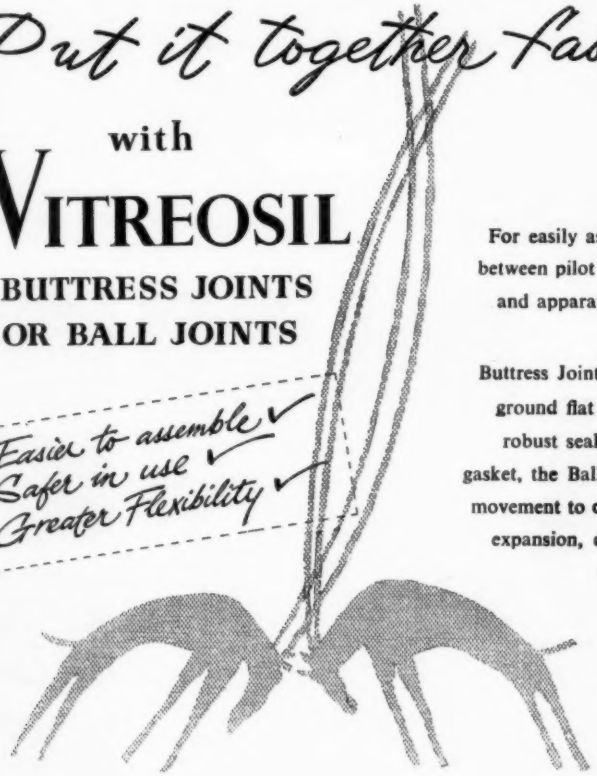

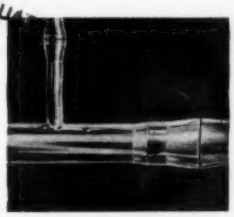

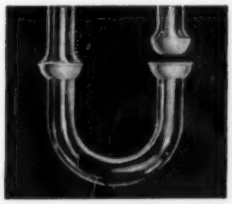

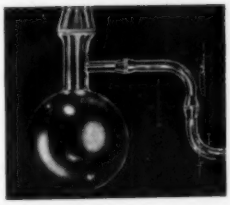

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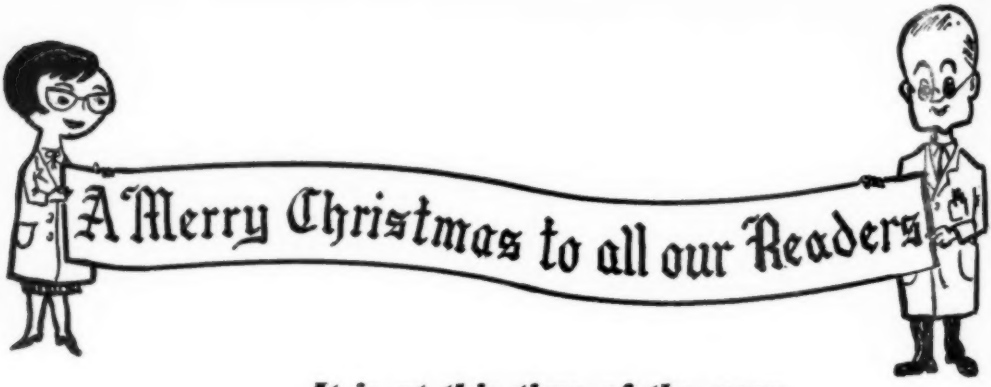

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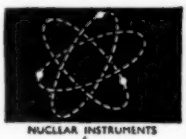
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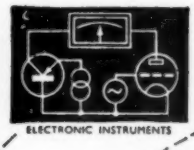
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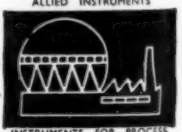
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NATURE

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Picture by courtesy of Douglas Lawson, F.I.B.P., F.R.P.S., F.R.M.S., F.Z.S. Author of 'The Technique of Photomicrography'

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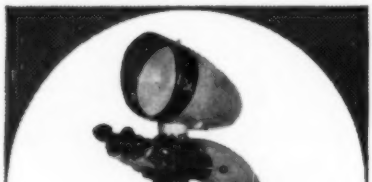

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PROSPECTS FOR EDUCATION IN BRITAIN

THE debate in the House of Commons on H.M. the Queen's Address from the Throne was notable for the choice of education for a full-day debate on November 7, and in speaking in the debate the Minister of Education, Sir David Eccles, said that he thought this was unprecedented. Sir David covered many aspects in his speech, beginning with a reference to the public library service. He had hoped a Bill could have been introduced during the session, but further study had been found necessary; and there seemed to be agreement that a new Act could not come into operation until the reviews of the local authority boundaries had been completed. One difficulty was in determining the qualifications of a library authority. Sir David thought that the recommendations of the Roberts Committee would not do justice to some of the good work being done to-day, and that further examination from a technical point of view might help in reaching a larger measure of agreement among those with expert knowledge of the service. Sir David also said that the Government is considering its policy in relation to sport, which would take due account of recommendations coming from the committee under Sir John Wolfenden appointed by the Central Council of Physical Recreation. The Ministry of Education is spending about £8 million a year on playing fields, swimming baths, etc., for the schools and technical colleges being built under the regular education programme, and extra resources will be available for the youth service in 1962–63. He thought, however, that there is scope for more co-operation in the use of existing facilities. Sir David also mentioned that a handbook on Commonwealth studies, written by a group of H.M.'s inspectors of education, is being issued as a guide to a subject which he believed the House wished to see widely taught.

Sir David believes that everything possible is being done in Britain to get more teachers for schools. He does not think we could have increased earlier the number of places in the general teacher training colleges from 23,000 to 47,000; the present programme came on top of the building programme for schools and technical colleges, which was already stretching the resources of many local education authorities. Colleges of 500 places and more have already been authorized in London, Loughborough, Coventry, Leeds, Sheffield, Exeter, the Liverpool area and in North Wales, and entirely new colleges are to be built in Cardiff, Canterbury, Brighton and in the Nottingham, Oxford, West Midlands and other areas. Of the places so far approved, 60 per cent will be provided by local authorities and 40 per cent by the churches and voluntary bodies, and Sir David paid a tribute to the part played by the churches. He also welcomed the prospect of a greater number of graduate teachers, and, with the expansion of the universities, he hoped that more graduates, particularly women, would teach in the primary schools. He believes that our aim should be to establish a two-way link between the training colleges and the universities. Something should also be done about the wastage of women teachers, and a campaign on a national scale to learn more about the availability of the 50,000 or more qualified women teachers who had left the service but had not reached the age of retirement would reach its peak in the new year. The pattern of part-time teaching also requires study, and he hoped for some thorough research into this subject by one or two local authorities.

As regards the supply of graduates, the Government is giving much thought to the development of full-time higher education as a whole, and the Prime Minister is to make an announcement very shortly as to this inquiry. Neither Sir David Eccles nor Mr. John Maclay, Secretary of State for Scotland, replying on the debate, would commit the Government as to whether or not there would be a separate inquiry for Scotland. On university awards, Sir David repeated the earlier announcements regarding the eligibility of a student for an award if he got a place at a university and had two passes at Advanced Level in the General Certificate of Education, the abolition of State scholarships after the selection to be made in the summer of 1962, and the retention of up to £100 a year by winners of open scholarships and other university awards. As a result, he hoped to see the foundation of scholarships at provincial universities, and he would shortly announce a radical revision of the means test, which, he said, has proved to be a more complicated matter than anticipated.

Referring to technical education, Sir David said that students taking full-time and sandwich courses at the colleges of advanced technology have risen from 4,000 in 1955–56 to nearly 8,000 in 1959–60, and an increase to 14,000 in a few years is expected. He is also anxious that these colleges should vigorously develop applied research, and that all technical colleges should develop as centres of further education in the widest sense, serving the whole of the community in their area. Sir David noted that these colleges are drawing their students from all types of school, but he pointed out that the biggest problem is that of students between the ages of 15 and 18, and how many are not getting the education we wish to give them. Although nearly 500,000 students are benefiting from day release, the annual rate of increase has slowed down, and important decisions must be taken between possible lines of advance. It has been

decided to give priority to reducing the size of classes in schools, but discussions with the local education authorities and industry regarding day-release have commenced in a promising atmosphere. However, he pointed out that we may sooner or later have to choose between placing the primary responsibility for training young workers in industry and the French system under which about a third of their young people receive their further education and initial industrial training before entering employment.

In concluding, Sir David referred to the urgent need for more and better technicians. He said that the Ministry has during the past year been reviewing, reconstructing and bringing up to date the whole pattern of courses for some 500,000 technicians, craftsmen and operatives. He also referred to the wastage in further education and said that it should be possible to reduce this drastically, though not to eliminate it altogether. Sir David also mentioned that detailed proposals for technical education will be announced shortly.

Although there was some sharp criticism of the Government's educational programme in the debate, this was mainly on party political lines, and comparatively little that was constructive emerged. Mr. A. Neave suggested that Britain needs much better criteria as to the numbers of scientists and technologists required, and Mr. J. Boyden thought that the Chancellor of the Exchequer and the Minister of Education should have concerted lines of development and seen that the University Grants Committee is provided with adequate staff to work out plans for the expansion of university and technological education. He also commented on the importance of the universities themselves doing more to explain their policies and ensure public understanding and support.

Particular attention was given to the question of wastage; Miss H. Anderson, for example, pressed the point in relation to full-time education, on which she pointed out that very little research had yet been undertaken. A detailed analysis by Dr. D. MacIntosh of students in Fife holding bursaries had indicated a rate of failure of more than 16 per cent, compared with the agreed overall wastage of about 17 per cent indicated by investigations by Sir James Mountford at Liverpool, Dr. Malleson at University College, London, and by the University Grants Committee. Miss Anderson was also very disturbed at a rate of failure of 38 per cent in the science faculty as compared with 10 per cent in the arts faculty. Mr. W. Hannan ,was more concerned with the wastage in part-time education, and with the unsatisfactory position of day-release in Scotland, and Mr. John Maclay, in replying on the debate, agreed as to the need for more careful study of the causes of wastage. He also agreed that Scottish industry as a whole does not appear to recognize the contribution which day-release could make to the training of young employees; the number of day-release students in Scotland has risen from about 28,000 in 1955–56 only to 35,600 in 1959–60; but it is intended to provide 100,000 places in Scotland by 1965, and the opening of the new technical colleges should stimulate development.

Many of the points raised in the debate, particularly regarding university expansion, the functions of the technical colleges, etc., are clearly matters which will be referred to the inquiry into further education as a whole; and there was a welcome disposition in the debate to look at education in the broadest sense, though it would undoubtedly be to the advantage of all if there was less disposition to seek party political or even sectional advantage.

JET PROPULSION ENGINES

Jet Propulsion Engines

Edited by O. E. Lancaster. (High Speed Aerodynamics and Jet Propulsion, Vol. 12.) Pp. xvii+799. (London: Oxford University Press, 1959.) 140*s*. net.

THE teaching of up-to-date aerodynamics has always been hampered by a dearth of good text-books and reference works. The main reason for this has been the very high rate of progress in all branches of the field, due to the vast resources which the major countries have invested in the development of aeroplanes; the impetus being mainly from the military pressure of two World Wars. The output of data has consequently been immense, and while much of the information has been disseminated in the publications of various specialized bodies, such as the Aeronautical Research Council and the Royal Aeronautical Society in Britain and similar bodies in other countries, the sheer volume of printed reports has made it difficult for the young scientist or engineer to obtain a good grasp of the subject. To add to his difficulties, a large proportion of new aeronautical information has always had a military security value in the country of origin, and there has therefore been delay, sometimes serious, in its open publication.

It is therefore highly desirable to attempt to make periodically a review of the 'state of the art' in aeronautics, and the need for a really vigorous attack on the problem led to the formation in 1949 at Princeton University of an Aeronautics Publication programme which has culminated in the publication of twelve large volumes, treating in both a comprehensive and fundamental manner practically all aspects of aeronautics and jet propulsion and such allied sciences as thermodynamics, physics of matter, nucleonics and so on. That the editorial board consisted of Profs. Theodore von Kármán, Hugh Dryden and Sir Hugh Taylor guaranteed the high standard of the contributing authors, who were chosen on a truly international basis.

What has emerged is so huge that it cannot be referred to merely as a series of text-books. It is rather an encyclopædia of aeronautical knowledge and would be a valuable addition to most engineering libraries. Nevertheless, the very size of the work (each volume contains around 800 pages) and the large number of authors involved has meant that the publication has taken a very long time. It is noted, for example, that much of the material in the present volume was written almost ten years ago, and where it relates to performance data on actual engines is

therefore out of date. This would seem to be a failure of editorship. Either the book should have been brought up to date before publication or the obsolete material should have been omitted. It should be emphasized that this criticism may not apply with the same force to the previous volumes, which deal with the more fundamental and theoretical aspects of aeronautics.

Volume 12 is the last of the series, and deals with jet propulsion engines of all types, including rockets and reactor heat sources. It also includes some very valuable and useful information on the ground test facilities which are so necessary in the development of these types of engine. It is a very comprehensive and on the whole a well-written work.

In particular, the sections on solid- and liquid-fuelled rockets are small text-books in themselves, and will be excellent as introductions into a field which until recently has been almost entirely military and therefore to a large extent security classified.

The chapters on ram jets, ram-jet test facilities and on the use of atomic energy for jet propulsion are equally good and well presented, although suffering from the general criticism of being rather out of date in parts. Special mention must be made of the discussion on ram-jet control, which is excellent, presenting alternative methods and showing how difficult it is to sense truly representative internal pressures or velocities in closed loop systems.

The very width of the field covered has, however, meant a somewhat restricted treatment of many subjects. The volume sets out to be comprehensive, but it loses comprehension in a different sense by failing to take individual topics far enough. Many of the theoretical treatments have been so generalized as to necessitate over-simple assumptions and too perfect conditions. None the less, with this limitation, the treatments are well done, and, for example, would be useful to a flight vehicle engineer who wished to compare different methods of propulsion or to a propulsion engineer who wished to consider a different field of propulsion. The generalized treatment again could, with advantage, have been extended to cover adequately the overall performance of engine/flight vehicle combinations over complete flight patterns or trajectories.

A real weakness in the volume is the inadequacy of those parts dealing with the future of jet propulsion. Such subjects as flight in excess of Mach number 3, high-energy fuel combinations, vertical take-off engines are only touched on in the most superficial manner. Section *L*, which is entitled "Future Prospects of Jet Propulsion", consists of an interesting account of the morphological method of analysis which, however, fails to demonstrate how the most promising future lines of progress should be chosen. Indeed, some of the thinking in this section appears to be amorphous rather than morphological.

In conclusion, Volume 12 of the series is a considerable effort by a large number of distinguished scientists and engineers. Whether, turning to the preface, it succeeds in meeting "the long-felt want in Research Institutions, Universities and private industry" would be a matter of some doubt if the decision had to be taken on this volume alone. My opinion is that a full set of these volumes would be invaluable to those libraries which have sufficient aeronautical readers to justify the high cost.

W. Cawood

APPLICATION OF LAPLACE TRANSFORMS

Laplace Transforms for Electronic Engineers

By James G. Holbrook. (International Series of Monographs on Electronics and Instrumentation, Vol. 10.) Pp. xiii+259. (London and New York: Pergamon Press, 1959.) 50*s*. net.

THE cult of manipulation without full understanding has achieved a degree of respectability since Oliver Heaviside made his remark about the necessity of eating even though the processes of digestion were not fully understood. He himself made full use of his own operational calculus without all the steps in it having been established with full mathematical rigour. It is indeed almost axiomatic that much progress in science and engineering is made by groping in the dark, and full understanding comer later, if at all. What is more controversial is whethes it is desirable to teach the use of a technique, which is already fully and rigorously established, without, at the same time, explaining fully the steps on which the technique is based. The busy engineer, faced with the necessity of solving a particular problem quickly, may well feel justified in making use of the latest technique, without fully acquainting himself with the rigorous mathematics necessary to justify it. But should instruction of the student be based on the same principle of quick results? The mounting pressure of new subjects on an already crowded syllabus provides a great temptation to make the treatment of all subjects more superficial in order to introduce students to as many subjects as possible in the hope that a full understanding of the subjects of most use to him in later life will be acquired by detailed work after graduation.

Mr. Holbrook is in no doubt of the importance of a thorough study of the subject of Laplace transforms, and has the courage of his convictions to the extent of facing the possibility of this subject being excluded from the undergraduate course, rather than let it suffer from an unduly compressed course of instruction. He does not, however, insist on complete rigour, and there are places in his book where some additional rigour could be introduced with advantage, possibly by means of extended footnotes, which could be omitted during a first reading.

The first two chapters of the book deal with functions of a complex variable and the Fourier series and integral. These chapters might well prove difficult reading for a first study of Laplace transforms, but the advantage of this approach is very clearly seen in the third and following chapters, where the author establishes his transformations and transformation theorems with great ease.

The last half of the book is concerned with the application of Laplace transforms to circuit problems. Much of this is extremely interesting and valuable, but seems to lack the unity of presentation of the first half. Although the author deplores the reluctance of engineers to use nodal analysis and their fear of problems involving mutual inductance, mesh analysis is employed in most of the problems given in the book, and mutual inductance is not mentioned until the last quarter of the book where five pages are allowed for its treatment.

Apart from this lack of balance the book is most attractively written, and the arrangement of problems

in the text in preference to placing them at the end of each chapter, should encourage the student always to arm himself with pencil and paper when reading. The contrast between print and paper is restful to the eyes, but the diagrams are too small. Mistakes are few, and only on p. 140 would they be likely to mislead the student. The lay-out of the mathematics is good and there is a table of more than 200 transformations.

This book should be a useful addition to the library of many engineers and students.

A. H. M. Arnold

THE NUMBERS GAME

Electronic Computers

Principles and Applications. By T. E. Ivall. Second edition. Pp. viii+263 (32 plates). (London: Iliffe and Sons, Ltd.; New York: Philosophical Library, 1960.) 25*s*. net.

Computer Engineering

Edited by S. A. Lebedev. Translated from the Russian by Jane Stuart. Translation edited by J. P. Cleave and F. A. Sowan. Pp. vii+184. (London and New York: Pergamon Press, 1960.) 63*s*. net.

Analogue and Digital Computers

Consulting Editor: Dr. M. G. Say. Advisory Editors: A. C. D. Haley and W. E. Scott. Pp. viii+308+12 plates. (London: George Newnes, Ltd., 1960.) 50*s*. net.

Introduction to Electronic Analog Computers

By Prof. John N. Warfield. (London: Prentice-Hall Electrical Engineering Series.) Pp. ix+175. (London: Prentice-Hall International, Inc., 1959.) 30*s*.

COMPUTERS are assuming an ever-increasing importance in the modern world. Having started as the plaything of the mathematician in the cloistered bowers of universities, they have successively penetrated into industry, commerce and, finally, they are likely to find a place in the government of nations. A measure of this increase in computer popularity is the almost exponential increase in the number of books on computers which have been and are being published.

A decade or so ago most authors started their book with a preface in which they explained why they had written the book, quite often couched in apologetic tones and usually with some cogent argument to justify their labours. Such literary politeness seems, however, to be a thing of the past and authors nowadays tend to give no reason to justify their effusions. In fact, a book may be justified on several counts. In the first place, novelty. The pioneers in a subject, if they have the time, can often write the first book which is available. Such books are useful in that they make available material which may only otherwise be found in the more esoteric literature. After this phase of development, the most likely reason for writing a book is that of popular exposition, since the original works may either be difficult intrinsically or alternatively have been succeeded by pedagogically better expositions and so have become unsuitable for teaching. In the case of the volumes under review, these two classes of book are represented and also the rather less desirable class of book, which presumably is written for no other reason than the desire of the author or publisher to 'get on the waggon'.

To deal first with the book by Ivall, this is in fact a second edition of the original book which appeared in 1956. The original work consisted of an edited version of a number of articles which appeared in *Wireless World*. The book has now been brought completely up to date, and something like a hundred pages of new material have been added. It is a book intended more for the wireless 'ham' rather than for the pure scientist or for the man in the street. There is a limited amount of technical material, but not enough, however, to build a computer, and too much to be intelligible to anyone who is not familiar with modern electronics. To the class of reader who is interested in electronics without being a specialist in computers the book can be recommended; to others, however, there are better things available.

Lebedev's book is in a different category. It is a translation of a Russian book which appeared in 1956, and deals with a number of aspects of computer design on an advanced technical basis. There is no concession to popular exposition, and the papers contained in the book are in the nature of a research collection. There is an account of the power supply for the Russian machine *BESM*, an analysis of digital differential analysers, an account of dynamic flip-flops and their use in computers, papers on automatic checking and on word selection from a dictionary (the latter based on a paper by me, which appeared in *Nature* in 1955) and two papers on matrix storage. For those Western workers in the computer field who do not read Russian, this book will be essential. Unfortunately, the price is high, considering the production, which is in lithographed, unjustified typescript; but even so, the good things in it make it well worth the money.

The collection of papers edited by Haley and Scott is, like the curate's egg, good in parts. There is an introduction to computing machines which did not appear to me to be particularly well written, three chapters dealing with the operation, application and design of analogue computing machines: these are excellent, although it is perhaps unfortunate that they are written by two separate authors with consequent breaks in style and gross overlapping. These are followed by an account of the way in which digital computing machines are operated. Part at least of this is a repetition of the first chapter, but considered as an introduction it is considerably more readable. The book ends with chapters on circuit elements for computers, on storage, on input–output equipment and on programming. The chapter on storage is dated and follows well-trodden lines, repeating several things from earlier books which have now been shown to be incorrect. That on input–output equipment is a reasoned and up-to-date account of what is available in this field, but the final chapter on programming is too short to be really worth while. This book is quite expensive for what it contains and the dichotomy of styles makes it somewhat difficult to read. It does not appear to add anything which will be of interest to the specialist, and, at the same time, is too advanced for the man in the street.

The book by Warfield has a somewhat misleading title, since, apart from a very brief introduction, in which a verbal account is given of the nature of digital and analogue computing machines, it contains nowhere any indication of the engineering details of an analogue computing machine. It is, in fact, a book which is primarily concerned with the programming of differential analysers. Considered as

such an account of programming it is one of the best books available on the subject. The techniques proposed are clearly set out and justified by sophisticated mathematics of a type which is not usually given in books on analogue computation. Apart from statements as to the way in which analogue computers are used, there is a set of appendixes which give the bibliographies of analogue computer elements and analogue computer applications. These are reasonably up to date, but suffer from the usual defect of American books in that they ignore all the literature published outside the United States. Rather surprisingly, the book ends with some suggested laboratory experiments. These will be useful to the growing body of departments which have analogue computers and have to instruct students in their use. The book is well produced and reasonably inexpensive. It can be recommended to those interested in this art. A. D. Booth

INDIAN RESEARCH ON JUTE

Jute in India

A Monograph. By B. C. Kundu, K. C. Basak and P. B. Sarkar. Pp. xv+395 (47 plates). (Calcutta: Indian Central Jute Committee, 1959.) Rs. 30.

THIS book presents a most interesting and detailed account of the scientific and economic research work on jute carried out under the ægis of the Indian Central Jute Committee over the past twenty-five years. It is divided into three sections, the first being concerned with the botany, cultivation, and diseases and pests of jute, the second with the economic and marketing problems of jute growing, and the third describing the physical and chemical characteristics of the fibre, together with notes on the technology of jute manufacture.

The jute-manufacturing industries of the world consume nearly 2 million tons of fibre annually, virtually the whole of this being grown in the eastern States of India and in East Pakistan. Before partition of the sub-continent in 1947, jute was a monopoly crop for India; after partition, although India retained the jute mills, most of the fibre-growing regions went to Pakistan. In consequence, the jute-manufacturing countries outwith India now find themselves largely dependent on Pakistan for supplies of raw material, while India herself has striven to increase her acreage under jute sufficiently to maintain the volume of her production of jute manufactures independently. The book is solely concerned with the Indian aspect, but it is against this wider background that it will be read in Britain and Europe.

Commercial jute is a bast fibre obtained from the *capsularis* and *olitorius* varieties of *Corchorus*. It is an annual crop, commonly followed by a crop of transplanted paddy, and in the first section of the book Dr. Kundu brings out very well the main factors of importance in growing and cultivation. All concerned with the production of jute, or indeed any bast fibre, will find much of value here. It is perhaps notable that the agricultural methods described are entirely manual, no power-driven machinery being employed.

Most jute growers are small-holders, and a considerable number share-croppers who pay a share of the crop as rent of their plot of land. In section two Mr. Basak describes the economic studies which have been made into the circumstances of these small farmers, many of whom appear to live barely above subsistence-level. His comments and conclusions on the economic factors affecting the marketing of jute fibre must give food for thought to all concerned with the jute industry, and it is especially interesting to note the correlation between acreage under jute and the relative prices of jute and rice in the previous year.

The final section, by Dr. Sarkar, is somewhat condensed, and, although useful for reference, seems unrelated to the main theme of the preceding sections.

The book contains more than 400 references, the majority to Indian publications, and 75 photographs, one un-numbered and without legend. There are a few errors in the text, and throughout Indian weights and measures are used which may be unfamiliar to many readers. Unfortunately no index is provided, a serious omission in a work of this nature, which could serve as a useful reference book. These criticisms apart, however, the monograph is a welcome addition to the sparse literature relating to this fibre of world-wide usage.

H. P. Stout

IN PURSUIT OF ANTIBIOTICS

Search for New Antibiotics

Problems and Perspectives. By Prof. G. F. Gause. (Trends in Science, Vol. 2.) Pp. x+97. (New Haven, Conn.: Yale University Press, 1960.) 4.75 dollars.

SINCE penicillin was developed as a commercial product there has been a feverish search for other antibiotics with similar or complementary properties. To-day, about a dozen antibiotics are in general use. Their discovery has been based on a purely empirical screening programme in which millions of potential antibiotic-producing organisms have been examined. Anything that could introduce a rational element into this search would be invaluable. Prof. Gause attempts to do this, and for this alone his book is worth study. His views are based on recent Russian research not too well known in Britain; it is useful to have an account of this work in English, and Prof. Gause is to be congratulated on the clarity of his exposition in a foreign language.

The author suggests that there are three principles by which the empirical search can be made more scientific. The first is concerned with the ecology of antibiotic-producers. He presents evidence that among fungi and spore-forming bacteria antibiotic-producers are more commonly found in warm soils than in cold northern soils. This could be a consequence of the richer microflora of tropical and sub-tropical soils. On the other hand, antagonistic Actinomycetes seem to be equally common in soils from all latitudes. My impression is that at present it would be premature to concentrate too much on soils from one climatic region in the search for new antibiotic-producers. But with Prof. Gause's general conclusion, that further study of the ecology of antibiotic-producers may make the search more rational, I wholeheartedly agree.

His second principle is that a given species, or other appropriate taxonomic unit, 'tends' to produce the same antibiotics whenever it is isolated, and that in consequence, rapid identification of organisms can accelerate screening procedures, preventing to some extent the continual rediscovery of a known antibiotic. If such a procedure were used too rigidly of course new antibiotics might be missed. This principle would be most useful where fungi and bacteria are being screened; in the case of Actinomycetes, identification of the antibiotic produced may frequently be more certain and more rapid than identification of the producing organisms.

His third principle is that test organisms used in screening procedures should include some chosen to detect selective inhibition of specific biochemical mechanisms. Prof. Gause illustrates this by his own work at the Institute of Antibiotics, Moscow, using mutant bacteria and protozoa with impaired respiratory pathways. He considers that these are in some ways analogous to tumour cells, basing this view on the work of Otto Warburg, and therefore proposes the use of such mutants in screening for antibiotics with anti-tumour properties. It seems to me somewhat naïve to base a search for anti-tumour substances on so simple a biochemical lesion in the test organism. Nevertheless, the data presented on their specific sensitivity to known tumour inhibitors are suggestive. But, whatever one may think of this particular instance, the general principle, that test-organisms with known biochemical lesions may be valuable in the search for antibiotics with specific properties, is undoubtedly valid.

In conclusion, though there is much in this book that is controversial, and much that one feels inclined to treat with reserve until more evidence is available, it is stimulating reading, and should be read by everyone interested in antibiotics.

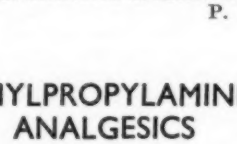
P. W. Brian

DIPHENYLPROPYLAMINES AS ANALGESICS

Synthetic Analgesics

By Paul A. J. Janssen. Part 1: Diphenylpropylamines. (International Series of Monographs on Organic Chemistry, Vol. 3.) Pp. vii+183. (London and New York: Pergamon Press, 1960.) 45*s*. net.

THIS book is the third volume of the International Series of Monographs on Organic Chemistry, edited by D. H. R. Barton and W. von Doering. The series is intended to cover a wide variety of aspects of organic chemistry in the form of concise summaries containing all relevant literature references. It is with this premise in mind that the book should be read, since it deals with a rather specialized topic, namely, the role of diphenylpropylamines of the type:



in the analgesic field.

It is an astonishing fact that although the analgesic methadone, which possesses the diphenylpropylamine structure, was discovered by the original German workers in this field during the Second World War, an apparently unabated stream of related compounds displaying not only analgesic but also a wide variety of other pharmacological activities has been appearing ever since. It is against this background of intensive and prolonged research by Paul A. J. Janssen and many other workers in various countries that this book has been written.

The first two chapters are concerned with some ideas on the nature of analgesic activity and the relative potencies of four of the best-known analgesics. The next sixteen chapters each deal with the synthesis and properties of compounds with one variant of the group *R* and are rounded off by a chapter on a few less-important variants. There follows a small chapter on dissociation constants, which have been regarded as being of possible significance in the activity of such compounds. The book is completed by a brief treatment of the work of A. H. Beckett and his collaborators, who postulate that the absolute configuration of all analgesically active optical isomers is identical and related to the configuration of D-(−)-alanine.

A valuable feature of the book is a tabulated survey of physical properties and analgesic potency ratios, measured against a few well-known analgesics, of all the diphenylpropylamines reported in the literature. That the main tables cover about 100 of the 183 pages of the book gives some idea of the tremendous amount of work done in this field. Despite this, the author is frequently able to suggest further areas of research.

The accuracy of a book so full of facts requires much time to check, but spot checks and my personal knowledge of the subject revealed no gross deficiencies, either in subject-matter or literature references. There are a few minor errors. For example, on p. 111, during a discussion on preparative methods, there is some confusion of nomenclature, formula 7.4 on p. 123 has a vital bond missing, the description of the reaction sequence on p. 120 is confused by an incorrect formula reference, "amine" instead of "amide" appears at the beginning of Chapter 11, ref. 87 on p. 132 should be 88, and '*J. Org. Chem.*' is omitted from ref. 317. However, in general, the errors are obvious and do not detract from the readability of the book. The correlation between the tabulated compounds and the structures discussed in individual chapters could possibly have been improved by the use of a common numbering system, but no great difficulty is involved on this score.

Dr. Janssen has written a thoughtful, analytical book which, although well confined to the subject-matter of the title, gives several glimpses of the many other pharmacological activities which modification of these propylamines produces. The reader may well detect a hint of the excitement which can be experienced during the investigation of structure-activity relationships in a successful line of research.

The book is recommended as being of value to the increasingly large number of those concerned with medicinal chemistry, as a concise method of following the work in this field. In addition, apart from its general interest, a number of chemically interesting points make it worth the attention of other chemists.

J. W. Billinghurst

The Great Barrier Reef and Adjacent Isles

By Keith Gillett and Frank McNeill. Pp. xiii+194 (161 plates). (Paddington, Sydney: Coral Press, Pty., Ltd., 1959.) 70*s*. (Australian).

TOURISTS with an interest in Nature will find all that they can desire in this book on the Great Barrier Reef of Australia by Keith Gillett and Frank McNeill. This is a first-class naturalist's guide book starting with a brief introductory account and taking the visitor first to the southerly Capricorn–Bunker group of islands. Then follow an account of the animals and plants to be found on land, an introduction to corals, and chapters devoted to molluscs, echinoderms, crustaceans, and other of the more striking reef inhabitants. This prepares the traveller for a journey farther north to the Cumberland group and other islands where a similar fauna will be found. An account is also given of Lord Howe Island and the Admiralty Islands.

There are other chapters on the resources of the reef, and the technique of underwater photography, together with practical hints for reef visitors. The book is well supplied with maps, and has good indexes to subjects and scientific names. It also includes mention of travel and tourists' facilities, including the underwater observatory at Green Island off Cairns. The interesting narrative is illustrated with superb photographs, many of which are in colour. The Great Barrier Reef is famous for the variety and splendour of its living organisms, and many of these are most beautifully portrayed. In fact, with this book the visitor can identify with certainty most of those animals which by their striking colour or form at once attract the naturalist's attention. The authors and publishers are to be congratulated on producing an authentic and beautiful handbook and guide, suitable for professional, as well as amateur, biologists, which will undoubtedly increase the enjoyment and value of a visit to the reef. It should also be in the library of those biologists not fortunate enough to go and see for themselves.

F. S. RUSSELL

Proceedings of the International Conference on Scientific Information, Washington, D.C.

November 16–21, 1958. Vol. 1: Pp. xxiv+1–812. Vol. 2: Pp. xii+813–1635. (Washington, D.C.: National Academy of Sciences—National Research Council, 1959.) 20 dollars the two volumes.

TEN years after the Royal Society Scientific Information Conference, the International Conference on Scientific Information, sponsored by the National Science Foundation, the National Research Council—National Academy of Sciences and the American Documentation Institute, was held in Washington in November 1958. All the Conference papers were issued as preprints to those who attended, but these are now re-published in two handsome volumes, together with additional material consisting of a memoriam to Dr. Alberto Thompson, who died before the Conference but who did so much towards its preparation, a preface by Dr. Wallace Atwood, jun., and the stimulating and scintillating opening address given by Sir Lindor Brown, one of the secretaries of the Royal Society. Moreover, the volumes contain the collected wisdom of the deliberations of the discussion panels and, in some instances, reports of the Conference discussions; there are also a list of those who attended and an index.

The papers cover the literature and reference needs of the scientist and their effectiveness, abstracting services, the organization of information services and storage and search systems, and the responsibilities of Governments and others in these fields. Some are verbose, some inconclusive, but there is much worth reading and pondering over. No rigid recommendations were made by the Conference, but, as Dr. Atwood remarked at the time, "'tis better to travel hopefully than to arrive". Scientific information bristles with complex problems, and while we travel hopefully towards their solution, the arrival of this important contribution to the literature is welcome.

C. A. RONAN

Lehrbuch der Physikalischen Chemie

Von Prof. John Eggert. Achte, neubearbeitete Auflage. Gemeinsam verfasst von Prof. John Eggert, Prof. Lothar Hock und Prof. Georg-Maria Schwab. Pp. xii+891. (Stuttgart: S. Hirzel Verlag, 1959.) 72 D.M.

THIS well-known book has been extensively revised and enlarged as compared with the English translation, and has to some extent lost its character as a readable elementary work and become a concise treatise on all branches of physical chemistry. Very recent work has been incorporated and there are abundant cross-references printed in the margins. References to literature are not given, apart from a list of books, mostly German and American, at the end, but the names of authors and the dates given will enable the publications to be traced in the abstract literature. The text is clearly and concisely written, and the mathematics is confined to elementary calculus. The sections on atomic physics and nuclear reactions are extensive, but the wave-mechanical theory of valency is only briefly treated. Experimental methods are dealt with concisely and there are many useful tables and graphs. As examples of modern topics the sections on low temperatures, semiconductors and reactions in solids may be mentioned. The chapters on photochemistry and colloids are good. The book covers all the branches of physical chemistry, and besides being a readable text-book it will be useful for reference purposes. The authors have evidently taken much trouble in the presentation of the material and the book will without doubt continue to be one of the best in its field.

J. R. PARTINGTON

Revision Notes on Biology for "O" Level of the G.C.E.

By G. T. Bolton. Pp. 17. (Oxford: Basil Blackwell, 1960.) 1*s*. 9*d*. net.

TO supplement existing text-books for the Ordinary Level examination in biology for the General Certificate of Education, G. T. Bolton, a biology master at Eton College, has prepared a set of notes which will be useful to all candidates in the twelve months before the examination. The notes include a number of lists and tables which the candidate can expand for himself into a full essay on the appropriate subject. The essential facts are briefly and boldly stated, but the notes can in no way be regarded as a substitute for a text-book. Some examination topics do not lend themselves to treatment in this way, and among the omissions are experiments which illustrate physiological processes in trees and plants throughout the year.

THE ROYAL SOCIETY

ANNIVERSARY ADDRESS*

By Sir CYRIL HINSHELWOOD, O.M., F.R.S.

AWARD OF MEDALS, 1960

Copley Medal : Sir Harold Jeffreys, F.R.S.

DURING the past forty-five years Sir Harold Jeffreys has carried out a long series of geophysical researches of fundamental importance. The problem of the internal constitution of the Earth involves many disciplines, and it was his outstanding achievement to take the existing scattered researches and weld them into the coherent subject now called the geophysics of the solid earth. His book, "The Earth", now in its fourth edition, is still the standard work in this field.

Jeffreys is best known as a theoretical seismologist. The Jeffreys travel-time tables, later revised in conjunction with K. E. Bullen, are not only the standard tables used in reductions of earthquake data but also are the basis of the best determinations of the elastic constants at all depths within the Earth.

He is the author of a number of papers on the radioactivity of rocks and the Earth's thermal history. Many years ago he emphasized the importance of making a deep boring through the ocean floor—a project which is now being undertaken by U.S. scientists. The interrelation of the phenomena of precession, nutation and the variation of latitude and the theory of the figure of the Earth led him to researches on these topics, and his analysis of gravity observations indicated a revision of the international formula for gravity, with a corresponding revised estimate of the Earth's ellipticity. The figures of the Earth and Moon formed the subject of his first paper in 1915, and in 1948 he gave a very important discussion of the general adjustment of the data relevant to the radius and ellipticity of the Earth, the lunar parallax and the moments of inertia of the Moon.

Jeffreys has carried out many researches in dynamical meteorology, and his classification of winds and his theory of monsoons are incorporated in the standard works on the subject. He extended the classical theory of the tides to atmospheric motions, and his work on the generation of water-waves by wind has led to many later developments.

His writings on the theory of probability and on scientific inference, his work on the asymptotic solution of differential equations and his systematic treatment of the Heaviside operational calculus have proved valuable. His continued interest in the problems of structural geology has helped markedly to close the gap that formerly existed between geology and geophysics.

Rumford Medal : Dr. A. G. Gaydon, F.R.S.

Dr. Gaydon is distinguished by his work in spectroscopy and particularly molecular spectroscopy. One of his main fields of research has been in the application of spectroscopic techniques to the study of flame phenomena. His studies of low-pressure flames, development of the nitric oxide test for atomic oxygen, measurements of rotational temperatures and discovery, with H. C. Wolfhard, of abnormal electronic excitation in the reaction zone, contributed much to knowledge of the processes occurring in combustion. Similar techniques have recently been applied to shock waves, and the shock tube has been developed into a tool for studying times of relaxation of molecular vibrations and dissociation.

Another main field of his interest has been the determination of the dissociation energies of diatomic molecules, and his book "Dissociation Energies and Spectra of Diatomic Molecules" is a standard monograph on the subject.

Gaydon has made many contributions in other branches of molecular spectroscopy as in the discovery of new band systems (for example, the ultra-violet $^1\Pi_u{}^1\Pi_g$ bands in N_2), the investigation of predissociation and laboratory observations of spectra similar to that of the night air glow.

Gaydon has also published "The Identification of Molecular Spectra" (with R. W. B. Pearse); "Spectroscopy and Combustion Theory"; "Flames, their Structure, Radiation and Temperatures" (with H. G. Wolfhard), and "The Spectroscopy of Flames". All these are distinguished works of much value and importance.

A Royal Medal : Prof. A. C. B. Lovell, O.B.E., F.R.S.

Much of our present knowledge of radio astronomy is due to Lovell's insight, initiative and originality. With his colleagues he has made contributions to our understanding of meteor astronomy and of 'discrete sources', and the conception and present achievements of the large radio telescope are largely due to his efforts. From visual observations it has long been known that meteors fall into two main classes. Shower meteors are clearly members of the solar system, but until the work of Lovell it was generally believed that the so-called sporadic meteors had velocities in excess of parabolic and were intruders from outer space. Lovell has been able to show conclusively that these objects too are members of the solar system, and further to show that the diurnal and seasonal variation in their numbers is consistent with such an origin. By his published works he has established the whole subject on a new and firm foundation.

Lovell and his colleagues have studied galactic radiation in the metre range. Fluctuations in this emission from certain constellations had suggested the occurrence of 'discrete sources'. Lovell was able to show that the fluctuations originate in disturbed regions of the ionosphere. It was found that the sources had diameters of a few minutes of arc, and thus

* Delivered at the Royal Society on November 30.

shown that the radiation did not originate in stars. Further work by Lovell's group showed that some of the discrete sources lie outside the galactic system, and that there is a roughly spherical halo well outside the visual system.

The conception and design of the large steerable paraboloid telescope are due to Lovell. Its construction represents the most significant advance in radio astronomy, and other larger instruments being built in different parts of the world are based upon it. It has proved invaluable for the tracking of stellar objects, but promises already to reveal much more about galactic radiation. Work on the 21-cm. hydrogen line is already providing much valuable information about the structure of the galactic system.

A Royal Medal : Sir Roy Cameron, F.R.S.

Sir Roy Cameron's chief interest over many years has been the mechanism of cellular damage by various agents and the response of the damaged tissue towards restoration of normal structure and function. His early work analysed the pathology of liver disease by resolving it into simple components related to the vascular system and to the excretory apparatus of the organ. This led on to a series of researches into the actions of various poisons which selectively destroy liver cells. His elegant study of the prolonged action of the chlorinated hydrocarbons provided experimental proof of the 'reversibility principle' in chronic liver disease, an achievement which has changed our outlook on some of the degenerative diseases which were once regarded as hopeless.

Cameron's investigations of body fluid redistributions in disease have added much to our knowledge of the causes of shock and of the pathogenesis of œdema of the lungs. He was the first to produce a neurogenic lung œdema, a discovery which helped to explain certain clinical phenomena that had long baffled surgeons. His war-time studies of arsenical and other poisons revealed unexpected modes of disease production and supplied a key for effective prevention and treatment. He has made important contributions to our knowledge of the mechanisms by which under-water explosions produce pathological effects, the practical result of which has been improved methods of care and treatment of men injured during diving and exposure to depth charges.

Cameron has built up a lively school of cellular pathology which has undertaken the critical re-examination of many of the classical notions about cellular disturbances and thus reorientated the outlook on diseases to which such disturbances give rise. He is recognized throughout the world as one of the foremost of living pathologists and has contributed much to revitalize British pathology by ingenious applications of the experimental method in problems of human ailments.

Davy Medal : Prof. J. M. Robertson, F.R.S.

When X-ray diffraction by crystals was first discovered nearly fifty years ago, it was a problem in optics and as such was studied almost exclusively by physicists. W. H. Bragg realized that since the compounds to be investigated would become increasingly complex, it would be advisable to have an organic chemist in his team of research workers. He therefore invited John Monteath Robertson to work at the Royal Institution ; and the distinction of the research work he did fully justified that choice.

J. M. Robertson proved to have just the qualities needed for the field of crystal structure analysis by diffraction techniques. Using the two-crystal moving-film spectrometer, and numerical and mechanical methods of Fourier analysis that he himself devised, he was not only the first to make a systematic investigation of the structures of such simple organic molecules as anthracene, naphthalene, durene and *p*-benzoquinone but also was a pioneer in the study of polymorphic structures (α- and β-resorcinol), *cis*- and *trans*-isomers (azobenzene), series such as dibenzyl, stilbene, tolane, involving bonds of varying order, or such as oxalic acid dihydrate, acetylene- and diacetylene-dicarboxylic acid dihydrates, where the existence of structural isomorphism is disguised by changes of unit-cell shape. He developed the 'heavy-atom' and 'isomorphous-series' techniques and used them to obtain the formulæ, stereochemistry and structure of the phthalocyanines, and later of cupric tropolone, the polysulphides and sulphonyl sulphides. He used structural data for the determination of molecular weights and (with others) investigated the effect of isotopic substitution and of thermal expansion in structures containing hydrogen bonds. His later studies of large condensed aromatic molecules and of compounds where steric hindrance forces an aromatic molecule to lose its planarity have provided valuable data for theoretical consideration.

Darwin Medal : Mr. E. J. H. Corner, F.R.S.

E. J. H. Corner first showed himself to be outstanding by his work in collecting and identifying toadstools. At the same time he developed a strong conviction about the advantage of studying plants in the wet tropics. In pursuance of this idea, he went to Singapore, where he worked for a good many years (including the period of Japanese occupation), and later worked in Brazil. The climax of his interest in toadstools was marked by his monograph on the great and exceedingly difficult group Clavaria. He found that he could recognize different systems of basic architecture in the growing tissues, and with this in mind he was able to organize what had seemed chaos into orderly sections.

His work on the huge fig genus, its classification, distribution and probable evolution represents work, on orthodox lines, but his studies on the evolution of tropical plants in general culminated in his celebrated 'Durian theory', which is still developing and may be deemed a major contribution to botanical thought.

This theory deals with the probable course of plant evolution in tropical high forest from remote periods down to the present time. He assumes that the main stream of plant evolution flowed in this environment, and then considers how the special features of this environment would favour particular kinds of plant organization. He concludes that the durian tree of Indo–Malaya represents the archetype of tropical forest tree—with its thick stem, large leaf, large seed, edible aril and other characters.

The Durian theory met with opposition, but is now widely referred to with respect.

Hughes Medal : Dr. J. L. Pawsey, F.R.S.

Dr. Pawsey is acknowledged as one of the pioneers in the development of radio astronomy. Soon after the War the Commonwealth Scientific and Industrial

Research Organization established a division of the Radio Physics Laboratory at Sydney, Australia, to carry out research work in radio astronomy, and Pawsey became the head of this division. Apart from many major personal contributions Pawsey has inspired a great variety of other fruitful investigations.

The Radio Physics Laboratory has carried out extensive work in both solar and galactic radio astronomy. At an early stage the principle of the Lloyd mirror was used to devise a radio-interferometer, the surface of the sea being used as the mirror. With this new device, some of the earliest evidence of the existence of the direct radio sources, radio stars, was obtained, and extensive studies of solar radio emissions carried out. Later, much more elaborate new interferometers with greatly increased resolving power were developed. The results are important for the understanding of solar terrestrial relations and include evidence of ejection of matter from the Sun during a period of intense radio emission.

Pawsey and his colleagues also continued the study of the galactic radio sources. By improved resolution they were able to identify some of the 'discrete sources'. Soon after the initial discovery of the emission of the 21-cm. hydrogen line, the laboratory began a detailed survey of the distribution of neutral hydrogen throughout the Galaxy, so far as could be undertaken in the southern hemisphere. Together with the work of Oort in Holland, the results have established the spiral character of our Galaxy. It was also soon established that the hydrogen line was emitted from an extragalactic object—the clouds of Magellan.

In addition to playing the leading part in these investigations, Pawsey has always maintained an interest in ionospheric studies and made an important contribution to knowledge of the lower fringes of the *D* region by carrying out reflexion sounding from a site in New South Wales, where the background noise was exceptionally small.

Pawsey, in conjunction with Bracewell, has written a standard monograph on radio astronomy.

OBSERVATIONS ON CELL MECHANISMS

It is five years ago to-day that I assumed the office which within an hour I shall be handing over. The intervening years have proved eventful ones in the life of the Royal Society. The Antarctic Expedition sailed to Halley Bay, made its distinguished contribution to the International Geophysical Year and returned, having written one more chapter in the Society's proud record of scientific exploration. Yet another chapter has been added by a biological expedition to one of the most interesting regions of South America. Although the future in this field is uncertain, progress has been made in the planning of space research in Britain.

When infused with true vitality, tradition is indistinguishable from progress, a truth which is apparent in many of the affairs of the Royal Society, and in none more than in our relations with our colleagues abroad. The historic friendship with American men of science, unbroken since the days of Benjamin Franklin, was movingly demonstrated by the National Academy of Sciences when it devoted one of its most important annual occasions to the honouring of the Royal Society Tercentenary and in the most cordial way invited your President to take part. Regular exchanges of students and lecturers with the Soviet Union have been brought into operation by agreements with the U.S.S.R. Academy of Sciences. I am specially happy to record that relations with the Academia Sinica, initiated last year by my own visit to China at their invitation, are developing in an encouraging way.

The whole field of international relations has been extraordinarily active, and I want to pay just tribute to the retiring Foreign Secretary, Sir Gerard Thornton, who has throughout so admirably performed the ever-growing duties of his office.

A practical body like the Royal Society is always conscious of the problem of ways and means. The Tercentenary Appeal and the establishment of the Wolfson Research Professorship have increased the resources with which the Society can meet its many obligations. If to-day we face the future with very substantially improved prospects, it is due to the energy and the vision of Sir William Penney, who retires to-day from the office of Treasurer, leaving the Society lastingly indebted to him.

The Tercentenary Celebrations are fresh in the minds of us all and I shall not recapitulate the many thoughts about the past and the future which were then expressed. But there is one thing which must be said, and that is to record gratitude to all who toiled so hard to make the events of the summer a success, and above all to Dr. Martin and his staff; and as far as I am concerned I must express my indebtedness not only in respect of last summer but of my whole term of office.

We have now returned to the workaday world of the new century, when we do well to remember again that the great themes of science emerge only after the accumulation of the results of many patient labours. I shall revert to some of those details now, and devote the rest of this address to some recent work on the biophysics of living cells which I have been able to follow at close quarters.

It has sometimes seemed to me that many people speak too much as though little mattered in living cells beyond the code inscribed in their nucleic acids, the mechanism of expression of this code in the cell properties being a relatively trivial affair. A change in the code is a mutation, and a convenient simplification ascribes all adaptive responses to mutations, ignoring the latitude which may exist in the translation of the code. But the detailed study of cells shows that there is in fact very much latitude. To quote one example, my close colleague A. C. R. Dean has recently studied the proportions of RNA, DNA and bacterial protein in cells grown under varied conditions. They vary widely, as does the cell size. There are clear evidences of oscillatory or 'overshoot' phenomena, suggesting a subtle and adjustable balance of interacting systems in mutual dependence. With change of medium the proportions of various enzymes in bacteria change very considerably, and enzymes are of course necessary for the synthesis of nucleic acid components.

The code-pattern of the DNA determines the cytoplasmic make-up. But, unless a non-physical kind of influence is assumed, Newton's Third Law suggests that in principle the cytoplasmic constitution might influence the DNA pattern itself. In other words, mutations normally attributed to accident might be induced, though this back action might be quantitatively small. In the synthesis of DNA the code must be spelled out in some polycondensation reaction.

At any stage of this process the alternative addition of a monomeric unit X or Y is believed to depend on what are essentially steric conditions. Yet these define a probability, not a certainty, and the normal course of addition could be modified by mass action factors coming into play if the changed cytoplasmic organization changes the proportions in which the monomeric units are offered to the growing points of polymers.

Thus there are several ways for unicellular organisms to respond to changed environment: quantitative readjustments in the proportions of cell components, gradually induced changes in the DNA code, and, as commonly assumed, selection of mutants formed by chance errors in the code and ousting the original forms by growing faster or surviving longer.

It has been widely asserted that the simple selection of chance mutants is the only true mechanism of adaptation. This view may have been based on an exaggerated view of what natural selection can account for, on some misrepresentation of Lamarck and on the failure of experiments on the so-called inheritance of 'acquired characters'. Perhaps also the unmistakable evidence that natural selection has operated has masked the fact that the variations selected may have had many kinds of origin and that there is no exclusive virtue in chance.

Not all biologists indeed adopt this attitude. T. M. Sonneborn, for example, discussing cell differentiation, remarks: "There is thus in general a marvellous system of give and take among certain genes and the cytoplasm" and he refers to "successive cycles of differentiation of cytoplasm by nucleus and then of nucleus by cytoplasm".

Experiments with unicellular organisms continue to show how manifold, subtle and unexpected are the phenomena of growth and adaptation, and fail to countenance the view that mistakes in coding are the sole source of advantageous variation.

Some years ago Akiba and afterwards Szybalski reported that cells in bacterial suspensions exposed to streptomycin were found after a time to be all dead or all resistant. This result was later re-interpreted by the idea that sensitive cells underwent lysis and were replaced by pre-existent mutant types which multiply on the debris. Similar objections were raised against F. J. Ryan's experiments on cells of *Escherichia coli*, which originally required histidine for growth but which on storage in a medium deficient in histidine gradually acquired the property of histidine-independence. Ryan, however, demonstrated that lysis and re-synthesis did not in fact occur. The proof consisted in showing that, in a medium containing lactose, the predicted shifts in the proportions of $(\text{histidine})^-$ $(\text{lactose})^+$ and $(\text{histidine})^-$ $(\text{lactose})^-$ are not observed as they should be if cryptic growth is the explanation. Ryan thinks that the DNA pattern changes during the stationary phase by some process other than a mistake in replication during growth.

Further light on the course of an adaptive phenomenon is thrown by the experiments of Midgley on the utilization of D-arabinose, and of N. Richards on the utilization of lactose by *Bact. lactis aerogenes*. The bacterium when first offered D-arabinose as sole source of carbon begins to multiply only after a lag of some days, which represents, according to one view, the time needed for internal adjustments in all the cells, and, according to another view, time needed for the multiplication, to the threshold of detectability, of a very minute proportion of abnormally coded mutants. Arguments, counter arguments and rejoinders beset this apparently simple theme. The new evidence is as follows. At various stages of the adaptation, enzyme activity tests (relevant to the utilization of D-arabinose) are made on unit mass of the culture. The measured chemical activity can, as a purely arithmetical operation, be divided either by the total mass of bacteria, or by the actual increase in mass since the adaptation started. In the first case the resulting quantity rises gradually and naturally to a limit as the exposure to the sugar continues and growth sets in. In the second case, which is appropriate to show the properties of the hypothetical mutants, the specific activity shows a most improbable course. Soon after the onset of growth it rises sharply to a very pronounced maximum from which it then rapidly falls again. The maximum is very much higher than is ever again found, even with the most thoroughly adapted cells. The mutants apparently acquire, just at the moment when they happen to be outnumbering the original non-mutants, a momentary activity far greater than they ever show again in the whole course of their history. If the idea of special mutants is abandoned, this strange behaviour is explained away by the simple fact that the chemical activity has been divided by the wrong quantity, not, correctly, by the total mass, but, incorrectly, by the increase in mass.

The subsequent history of the adaptive enzyme changes during prolonged cultivation in D-arabinose, and during alternate periods in arabinose and glucose reveals an intricate pattern of successive reorganizations. At first the arabinose-utilizing enzymes prove unstable to growth in absence of arabinose, and decline. But with longer adaptation to arabinose they do this less and less, and in a way which shows the whole conception of 'stable heredity' in adaptive changes to be complex and relative. According to the precise conditions of growth, the special enzyme may either decline or continue to be synthesized in the absence of the original 'inducer'.

All these facts give a powerful impression of a machine with intricately geared parts, of equilibria and quantitative balances about which by no means the last thing can be said in terms of mistakes in coding.

Cannon has complained of the confusion caused by mistranslation of Lamarck's word 'besoin'. This should of course be translated 'need', and, without entering into more controversial fields, I should like to point out that in adaptive studies the development of functions in response to needs is very much in evidence. For example, N. Richards, in his studies of lactose utilization, finds that as a culture of *Bact. lactis aerogenes* becomes short of oxygen the galactosidase activity increases. In the absence of oxygen, utilization of carbohydrate is less efficient: more is needed, and more is made available by the increase in enzyme activity. This is clearly a response to a 'need'. It is not mysterious. When the enzyme is insufficient, processes dependent on it are retarded relatively to its own synthesis, with the result that its proportion increases until a proper balance is established.

It is a quite general law for the reproduction of living matter that the reaction system tends to be established which gives the greatest growth-rate. This, it is worth while pointing out once more, is itself a form of natural selection, automatically operating to

favour the predominance of the most efficient systems. In the long run the selection of the best reaction pattern gives the same result as the selection of a special type of individual.

The orthodox view, however, is that such phenomena are of little significance beyond the generation in which they occur. On this several things may be said. Cannon has objected that most of the negative experiments on acquired character transmission have been of a rather crude kind, in which failure proves little or nothing. There is no doubt that the persistence of adaptive enzyme formation through many cell generations in the absence of the inducing agent is a very variable and complex story. The persistence may be great even where the evidence suggests that the original adaptation was not a mutation.

There are perfectly natural physicochemical mechanisms by which a changed cell organization could survive for many divisions of a unicellular organism returned to a previous habitat after an adaptive interlude. But, in addition to this, Newton's Third Law, as I have already said, discourages belief in the absolute inability of genetic codes themselves to be modified by the workings of the very systems which are built to their instructions, and by which, be it said, they themselves have to be reproduced. The gradual stabilization of adaptations is a very striking phenomenon, upon which I think we should ponder deeply. In his book "Brain, Memory and Learning", W. Ritchie Russell says, "All living matter shows features that may be considered a form of memory. It all shows spontaneous activities that tend to form patterns which are at first relatively simple, but show a strong tendency to repeat".

An interesting variation on the theme of stabilization is reported by Ierusalimski. A spore-forming organism (*Clostridium acetobutylicum*) was adapted in continuous culture for 21 days to resist the toxic action of 0·6 per cent butanol. After sporulation, the strain was no more resistant than a control. When, however, the adaptive treatment had been further prolonged and the butanol concentration gradually increased, the resistance not only rose but also could now survive passage through the spore form.

I shall now turn briefly to some of our own results on the resistance of micro-organisms to drugs, and will begin by repeating my belief that not one but several mechanisms exist for this phenomenon, and, in particular, that accidents of code replication are not the sole or even necessarily the most important source of resistance.

To find the proportion of resistant mutants a common method is to spread a very large number, N_0, of organisms on an agar plate with nutrient and with the drug at concentration c and to count the number, N_∞, of colonies that eventually develop. $N_\infty/N_0 = \alpha_\infty$ is the required proportion. More detailed investigation alters the picture. The colonies take different times to reach a standard size, and the proportion, α_t, rises with time from zero to α_∞ according to a curve indicating an approximately Gaussian distribution of development times. J. B. Woof has studied the phenomenon with *Bact. lactis aerogenes* and chloramphenicol. As the drug concentration increases, L', the time at which $\alpha_t/\alpha_\infty = 0{\cdot}5$, decreases, a rather paradoxical behaviour for mutants. With an adaptive hypothesis the paradox disappears. α_∞ is small because there is a race between adaptive adjustments and lethal processes which, given time, stop the cells from forming colonies at all. Calculation shows that if the logarithmic death-rate is λ, L' will in fact decrease as λ increases, that is as the drug becomes more potent. If the cells die quickly only those that make haste to adapt ever have a chance to form colonies at all. The successful ones are those in the tail of the statistical distribution. The fiercer the drug action the more the colony formation is confined to the exceptional members of the distribution. Woof's studies show that this picture works out quantitatively.

The conception of adaptive and lethal processes in competition may be thought difficult. The reality of such superpositions of conflicting processes is illustrated by some of Midgley's experiments on the adaptation of *Bact. lactis aerogenes* to D-arabinose. At the initial transfer to the pentose the lag is x days and the subsequent growth-rate r_1, which is far below the optimum. If the lag in arabinose is interrupted by passages in glucose during which growth takes place, the total value of all the lags in arabinose before growth occurs in it still adds up nearly to x. But, as a result of the intermissions for growth in glucose, the growth-rate in the arabinose is now much greater than r_1. During the long adaptation to arabinose other cell mechanisms suffer from ageing unless they are kept mobilized by the opportunity for use in the glucose medium.

In the competition of adaptive and lethal processes the situation might perhaps be likened to that of a man dying of destitution while he is struggling to finish a job which will furnish the means for his physical salvation.

Another approach to the problem of chloramphenicol-resistant colonies has been followed by Dean. If the drug concentration on an agar plate is low enough, every cell plated can form a colony. An inoculum from one of these colonies is spread on a plate with a slightly higher concentration of drug, and again the proportion forming colonies approaches unity. Proceeding carefully in this way, and sometimes spreading for several successive tests at the same drug concentration, we can arrive at colonies growing on plates with ten or twenty times the concentration which would originally have been completely inhibitory. At every stage of the process the yield is so high as to rule out all possible talk of rare mutants. Errors of coding which can occur every time, or even once in two or three times, would seem to be misnamed.

The most powerful proof that resistant forms can sometimes arise fortuitously comes from Lederberg's elegant technique of 'replica plating'. The principle, briefly, is that, by means of a suitable pad, multiple prints can be made from a given bacterial plate on to several others, with and without drug. Resistant colonies can be detected on the drug plates, and their opposite numbers on the drug-free plates isolated. By successive enrichment resistant strains can be obtained without previous direct contact with drug.

Lederberg obtained in this way strains resistant to streptomycin and to bacteriophage. By a modified replication technique Cavalli, however, could obtain only a small increase in chloramphenicol resistance comparable with what can occur as a result of varied cultural history. It seems, nevertheless, to be tacitly assumed sometimes that the replica plating technique can be quoted to prove the existence of mutants in cases to which it has not been applied at all. This is particularly inadmissible because both phage resistance and streptomycin resistance can arise from

damage, for example, by ultra-violet light, depriving the cells of receptors for the agents in question.

It has also been pointed out that the organisms isolated by replica plating are never known to be resistant until they have been tested in the presence of a drug. What has been selected, therefore, may be not so much a resistant form as one specially endowed with the power of responding rapidly when exposed to the drug, that is of doing what in other examples a large proportion of the population succeed in doing more slowly. This reflexion suggests the possibility that the differences in behaviour are not necessarily more than quantitative. Valuable information may thus be forthcoming from a more detailed study of the response to drugs of organisms selected by indirect means.

Discrepancies in apparent results often arise from unsuspected differences in method. It is therefore of interest to note that W. T. Drabble, by the same methods which have provided evidence for direct adaptation to chloramphenicol and other agents, has obtained results with streptomycin pointing clearly to the presence of some initially resistant forms of *Bact. lactis aerogenes*. There are also indications, which he will report in due course, of a superposition of direct adaptation upon a selective process.

In this last address from the presidential chair I have, as it were, returned to the laboratory by a deliberate choice. It was not that large general themes, scientific or otherwise, were lacking. I had perhaps reflected a little on a remark I heard recently from a young colleague to the effect that scientists tended to deal with broader questions when they were getting past work in their own field, but I am, I think, on good enough terms with my younger colleagues not to be intimidated by them. It was rather that, after the Tercentenary, it seemed better to strike the workaday note once more. Some of the views I have expressed may seem to verge on the heretical. They are not, I think, irreconcilably so. In a recent study which Bartlett and I made on the crossing of resistant and non-resistant bacteria, we reached some conclusions which at any rate one colleague in genetics welcomed as support for an orthodox view. The truth, I believe, is that we need a re-synthesis of some of the widely accepted views with the kind of approach that appeals more to the chemist and the physicist.

Be that as it may, nobody would expect an occupant of this chair to subscribe against his beliefs to orthodoxy. May I quote once more the words of Horace with which you are familiar:

> "ac ne forte roges quo me duce quo lare tuter
> nullius addictus iurare in verba magistri"

I hope the President himself may be forgiven for following this example.

To have been President of the Royal Society is, it seems to me, the greatest honour which any man can have received, and one of which no man can feel he has been worthy. For myself I can only thank those who have done their best to see me through. I welcome my successor and wish him well. There are plenty of problems ahead. For example, our long and, though informal, immensely important relations with the Government are in process of adaptation to the vast scale and complexity of scientific activity to-day. The optimum solution of this problem is of the greatest importance both to the Society and to the country. Of equal importance is the establishment among the Fellows of the right balance between the pure and the applied sciences to enable the Royal Society to maintain its full influence in the modern world.

I regard the future of the Society with confidence not least because I see no sign that it is likely to depart from the principle declared in its motto that it will remain "nullius in verba".

TREND OF CÆSIUM-137 IN THE EFFLUENT OF A LARGE CITY*

By Dr. T. R. FOLSOM
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AND
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THE oceanographer is concerned with the mechanisms controlling the dispersion of materials in the ocean. For this reason, the progress of fall-out radioactivity in the ocean has been studied for several years at the Scripps Institution; recently special consideration has been given to contributions coming from terrestrial run-off. Several radioactivities in sewage flowing from a large coastal city were monitored at the treatment plant for more than two years. Cæsium-137 was followed in detail; this fission product has useful tagging properties; it emits a penetrating, easily detectable γ-ray, and decays relatively slowly.

Detailed off-shore mapping has not yet been done; however, the average and peak outputs from the city have been recorded over a period of 21 months, permitting estimates of the influence on coastal waters. The character and trend of the concentration, and comparisons with reported contamination of human food by fall-out, point to an unexpected source for the cæsium-137 observed in the sewage. Not a great deal is known about the chemical behaviour of this nuclide, at very low concentrations and in complex systems, so that the partition observed for cæsium in the plant should be of general interest.

* Substance of a paper read in part at the meeting of the International Association of Physical Oceanography, Helsinki, Finland, on August 5, 1960.

We were fortunate in being permitted to make measurements throughout the Hyperion Treatment Plant of the City of Los Angeles. This modern installation is situated on the seashore 120 miles north of the Scripps Institution; it collects sanitary sewage from a large city centred about 30 miles inland; and disposes the treated material mainly through outfall pipes extending as far as 7 miles into the open sea where the depth is about 200 ft. Very little storm water enters this system.

For about ten years, until June 1, 1960, the treatment included primary settling, aeration with activated sludge, final settling, digestion of primary and activated sludge, followed by the filtering, washing and drying of part of the digested solids to produce a stable dry fertilizer that was sold as soil conditioner. After this date a change was made in the treatment scheme, so that routine drying of large amounts of fertilizer was stopped.

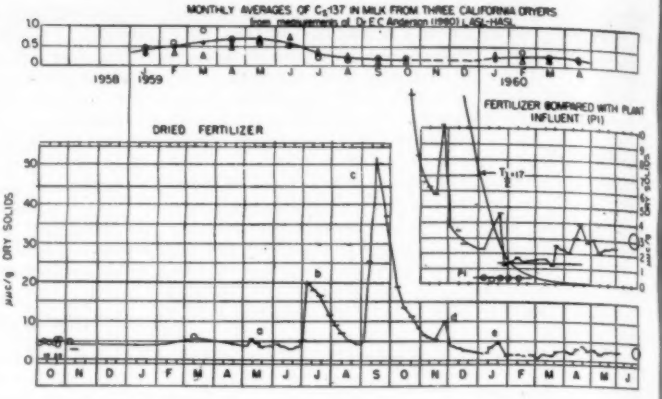

Fig. 1. Trend of cæsium-137 in the sewage treatment plant compared with the trend in milk. All ordinates are micromicrocuries per gm. of dried solids. Inset illustrates that batch inputs probably contributed little during comparisons early in 1960

Investigation at the plant consisted of: (1) sampling continuously and in detail at one point in the system; (2) sampling also at several points during a given short period, preferably when the input character was not changing rapidly. While it was available, the commercial fertilizer was used in the continuous monitoring; it was convenient, and because cæsium is greatly enriched by treatment up to this point, extremely small changes in input concentration could be deduced. These samples were assayed after being composited daily for periods of 3–5 days. Most of the other specimens used for establishing partition ratios were liquids, some of them very dilute. All were reduced to dryness at the plant in 40-gallon soup kettles heated with steam.

Assaying was done at the Scripps Institution by exposure of a sodium iodide scintillator crystal to the radiation from a relatively large specimen, one weighing about 200–400 grams. With a modern multichannel gamma-ray spectrometer a specimen may be analysed within a few minutes for one or more gamma-emitting nuclides, even when their concentrations are very low. Usually no wet preparation whatever was undertaken; however, specimens were assayed in plastic containers under uniform conditions, so that accurate comparisons with standard specimens could be made. The laboratory at Scripps had already developed a spectrometer accessory[1] permitting the rapid comparison of measurements with a library of background measurements and measurements of standard specimens all stored in digital form on magnetic tape loops.

In passing, it will be mentioned that the sewage had less radioactivity than was anticipated; no concentration was observed even approaching a recognized tolerance-level. Nevertheless, the natural background from the uranium and thorium families almost always was surpassed by one or more man-made activities. Iodine-131 appeared in nearly every input specimen as might be expected from its use in medicine; cobalt-60 repeatedly appeared in easily measurable amounts. Relative to the concentration of cæsium-137, the concentrations of both zirconium-95 and ruthenium-106 were extremely deficient when compared with the ratios observed in rainfall for this period. Details concerning these and other activities will be reported elsewhere.

Monitoring radiocæsium in digested material has several practical advantages; but because of the long dwell of material in digesters, the information is not contemporary, and some input detail is lost entirely. Fig. 1 shows the trend of cæsium-137 concentration over 21 months derived from 75 composited samples of digested fertilizer. The large peaks attenuate at a rate consistent with what is known about the purging-rate of these digesters. Actually a battery of digester units is used at Hyperion; nevertheless, their performance might be approximated roughly by a model having a single tank into which a daily input is suddenly injected and mixed thoroughly followed by the withdrawal of an equal amount, about one-thirtieth of the whole. It can be shown that this model would purge itself after a sudden excessive input to half-peak-concentration in about 21 days. The actual measured initial slopes of the two larger peaks correspond to a half-purging time T of about 17 days.

In spite of the large batch inputs, it appears from Fig. 1 that the input concentration varies only slowly much of the time and follows an easily measurable basic trend. It required roughly four months for attenuation of the largest batch, but ultimately this reached insignificance. An inset is shown in Fig. 1 magnifying the data for the first three months of 1960, and an exponential curve having half-value of 17 days has been added to it to illustrate that the largest peak and later smaller ones probably have become greatly attenuated during the period when input concentrations were compared with average concentrations in the digested material. These comparative measurements are plotted in the inset of Fig. 1 and listed in Table 1. From these roughly steady-state conditions we can derive ratios that should approximate fixed characteristics of the plant. Table 1 indicates that the incoming cæsium-137 is enriched after digestion by a factor of about 1·4/0·32 or 4·4 (on a dry basis).

It can be concluded from these measurements that the concentration of cæsium-137 in the sewage coming

Table 1. Comparison of Influent and Fertilizer Concentrations

Collection date of composite sample (5-day period ending)	Concentration of ^{137}Cs ($\mu\mu c.$ per gm., dry)
Dry fertilizer (after long digestion)	
January 27, 1960	1·2
February 2	1·4
,, 10	1·8
,, 17	1·5
,, 24	1·6
March 2	0·7
,, 9	1·8
Fertilizer average	1·4
Influent (composited 5 days and dried)	
January 6, 1960	0·39
,, 15	0·22
,, 22	0·48
,, 29	0·19
February 12	0·32
Influent average	0·32

into the plant fell slowly over 21 months from about 1·1 to about 0·32 $\mu\mu c.$ per dry gram; this corresponds to a change from 1·4 to 0·4 $\mu\mu c.$ per litre.

Now it can be appreciated why direct monitoring was not carried out. No satisfactory chemical precipitation had been developed; boiling down all specimens in barrel-sized amounts would have been expensive; and the spectacular enrichment in the digested material was attractive. For example, raw sewage having 0·4 $\mu\mu c.$ per litre of cæsium-137 produces dried fertilizer having 1,400 $\mu\mu c.$ per dry gm.

Obviously the large peaks in Fig. 1 arose from batch inputs. But no technical or medical practice has been discovered that would explain the slowly varying basic concentration-level. When measurements were made of representative samples from the city's major water supplies it was found that this source, too, was deficient. The average value measured for the fresh drinking water was only 0·025 $\mu c.$ per litre; this corresponds to only about 0·02 $\mu\mu c.$ per gm. of sewage (having 1,250 p.p.m. total solids), so that fresh water could contribute only about 6 per cent of the cæsium-137 observed in the sewage.

Anderson[4] has considered in some detail the available reports concerning U.S. national dietary habits, and by introducing values of cæsium-137 found in foods, he has ventured a rough estimate of the amount of cæsium-137 that was daily ingested per person in 1956. There are several reasons for concluding that the value he derived, about 50 $\mu\mu c.$ per day per person, would become no smaller if it could be corrected by deriving it from data pertaining to the spring of this year. If this value is tentatively accepted, and also if the estimates are taken that 2·8 million people contribute to a system carrying 250 million gallons per day and 1,250 p.p.m. total solids, then a possible daily input of cæsium is discovered that is much larger than could come through drinking water. In fact these, apparently conservative, values provide for roughly one-third of the average cæsium observed in sewage early this year. To this, of course, must be added a contribution from garbage now frequently disposed of through kitchen grinders in this community.

No attempt will be made to balance the budget precisely, but use here of a 1956 fall-out contamination value needs some justification. After 1956 world-wide fall-out increased in rate; later it decreased[5]. During the period of these investigations at Hyperion the concentration of cæsium-137 in dried milk from three nearby milk-sheds varied as shown at the top of Fig. 1. Milk is reported to be the largest contributor of cæsium-137 in diet, and the concentrations in dried milk reported for the spring of 1960 are not strikingly different from those reported for 1956. Between these dates there were higher levels in almost every food; and almost every food in practice experiences a lag before it is delivered and consumed. There is also a substantial lag that occurs between input and output of cæsium in the human system[4,6]. It would therefore appear necessary to correlate sewage concentrations not with contemporary food contaminations but with concentrations measured in foods produced several months earlier. Because of these circumstances, it appears quite possible that the basic trend of cæsium-137 in the Hyperion sewage could be controlled almost entirely by fall-out cæsium entering through human food.

In many circumstances cæsium behaves chemically and biologically like potassium, an essential tissue constituent; nevertheless there are several biological systems reported where a clear distinction is made between these two elements. In some cases, the discrimination has been observed to be against the intake of cæsium and in favour of potassium; for example, plants are reported to discriminate strongly against radiocæsium in taking the two elements up from the soil.

Concentration and digestion of sewage depends largely on metabolic processes, and much of the final solid material has been synthesized by microorganisms. Therefore, it was not anticipated that cæsium would become strongly concentrated in the solid digested fraction relative to potassium. Table 2 indicates that cæsium-137 is enriched relative to potassium by forty-fold during the reduction of sewage to digested, dried fertilizer. This aspect is being studied further.

Although it appears that the sewage system studied can collect the minute traces of fall-out cæsium passing through in human food, the effect on the sea

Table 2. Cæsium-137 to Potassium Ratio in Raw Sewage and Fertilizer

Date of collection	Fertilizer			Date of collection	Raw sewage		
	^{137}Cs $\mu\mu c./gm.$	K(total) gm./gm.	Cs/K $\mu\mu c./gm.$		^{137}Cs $\mu\mu c./gm.$	K(total) gm./gm.	Cs/K $\mu\mu c./gm.$
January 27, 1960	1·2	0·003	400	January 6, 1960	0·39	0·024	16
February 2	1·4	0·003	470	,, 15	0·22	0·031	7
,, 10	1·8	0·002	900	,, 22	0·48	0·029	17
,, 17	1·5	0·003	500	,, 29	0·19	0·012	16
,, 24	1·6	0·002	800	February 12	0·32	0·020	16
March 2	0·7	0·001	700				
,, 9	1·8	0·003	600				
Average	1·4	0·002	620		0·32	0·023	14

cannot be great. This is because surface sea waters have caught and have failed to dissipate downward such large amounts of fall-out that the concentration of cæsium-137 persists at levels not far below what is seen in average sewage. Measurements[2] made of the cæsium-137 concentration in the local surface sea water early this year by us, gave an average of about 0·1 μμc. per litre. This should be compared with the value of 0·4 μμc. per litre representing the average concentration in the Hyperion sewage at the same period.

It is useful to compare average concentrations in this manner, but it should be pointed out that even in specimens taken from nearby points in the open sea the concentration may vary by more than 50 per cent. Smaller average concentrations were measured[2,3] in local coastal waters than in waters far off this coast; and Yamagata[7] has reported the average concentration for 1959 Japanese coastal water of 0·38 μμc. per litre, or essentially what has been observed in Hyperion sewage.

Even the peak concentrations observed at this plant should cause no alarm. From plant characteristics, it may be estimated that the largest peak in Fig. 1 corresponds to a batch input of about 0·4 curie. However, the sewage travels on the average 30 miles to the plant and is not likely to pass through in much less than one day, and the 250 million gallons of water put through in one day would dilute this to an average concentration of only $3·7 \times 10^{-7}$ μc./ml. This falls far below the value of 2×10^{-5} μc./ml. now accepted as maximum permissible concentration for this particular isotope in water that is to be drunk continually by humans.

From these investigations something has been learned concerning the behaviour of radiocæsium in a large modern sewage disposal plant, and useful conclusions can be drawn concerning the probable influence on the downstream environment. It can be seen, for example, that the original objective of following the local dispersal of sewage by the ocean can be attained only if the most sensitive and refined methods are applied. It appears, too, that suitable monitoring of the gamma-ray activities in sewage systems might provide additional safeguards to the public against misuse of the radioactive materials that are becoming more and more common in research, medicine and in industry.

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OBITUARIES

Dr. J. M. Cowan, C.B.E.

With the sudden death of Dr. John Macqueen Cowan on the evening of October 26, after a very happy day with his friends on the Gardens Committee of the National Trust for Scotland, Scotland lost one of her most distinguished horticulturists.

A son of the manse, he was born in Banchory, Kincardineshire, in 1892, received his early education at Gordon's College, Aberdeen, attended the University of Edinburgh, taking the arts and science degrees with honours in botany, became an undergraduate at Oxford, reading honours in botany with Prof. Vines and Dr. Church and forestry with Sir William Schlich, before being appointed to the Indian Forest Service. At Oxford he met Adeline May Organe, who took an honours degree in botany, whom he married and who at all times was the source of the greatest possible encouragement to him; in fact, she was co-author of one of his earliest publications, "The Trees of Northern Bengal" (1929). In India he followed the example of some of his distinguished predecessors in the Forest Service, such as Brandis, Lace and Gamble, pursuing his botanical investigations as well as proving himself a forest officer of outstanding merit. It was not surprising, therefore, that from that Service he was chosen to officiate as superintendent of the Royal Botanic Gardens, Calcutta, the chief botanical post in the Indian Empire.

Retiring from India in 1928 and after undertaking, with Dr. C. D. Darlington, a botanical expedition to Iraq and Persia, on behalf of Kew and the John Innes Horticultural Institution, Cowan returned to Scotland in 1930 as assistant to Sir William Wright Smith, the regius keeper of the Royal Botanic Garden, Edinburgh. Soon he was deeply engrossed in the taxonomy of the genus *Rhododendron*, the genus which had fired the enthusiasm not only of his immediate chief but also of the professor who had lectured to him as an Edinburgh student, Sir Isaac Bayley Balfour. On the taxonomy of this complex genus he published widely, often in collaboration with his Edinburgh colleagues; he published, too, on the genera *Cyananthus*, *Roscoea*, *Wendlandia* and others, as well as on the history of the Royal Botanic Garden. At all times he took a keen interest in the welfare of the horticultural students in the Garden, and if at times the students were not altogether approving of some of his teaching methods, they were always appreciative of the generous hospitality of the Cowan household.

Late in the 1940's Cowan became deeply interested in the activities of the National Trust for Scotland.

and especially interested in the two great Scottish gardens the Trust took over—Crathes in Kincardineshire and Inverewe in Ross and Cromarty. He gave great prestige to the Trust when, under the Trust's auspices, he inaugurated the early 'Garden Cruises', a unique and previously unused method of transport which has enabled people from all parts of the world to visit famous, and sometimes somewhat inaccessible, gardens in great comfort.

Happy and industrious though he had been in India, and undoubtedly was in Edinburgh, he frankly admitted that not until he retired from Edinburgh in 1954 and accepted the post of gardens adviser to the National Trust for Scotland, with his headquarters at Inverewe House on the incredibly lovely and rocky peninsula at Poolewe, did complete contentment and satisfaction come to him; and naturally so, when through his great energy and drive he saw the number of visitors to the Garden steadily increase from a few hundreds in 1954 to 47,000 in 1960.

Cowan's services to horticulture were acknowledged by the Royal Horticultural Society by the award of the Veitch Memorial Medal in 1951 and by the Victoria Medal of Honour in 1955. He was made C.B.E. in 1952. Mrs. Cowan and a son and daughter survive him. H. R. FLETCHER

Prof. Yehuda Hirshberg

PROF. YEHUDA HIRSHBERG, head of the Laboratory of Photochemistry and Spectroscopy in the Weizmann Institute in Rehovoth, Israel, died on September 20. Prof. Hirshberg was born in 1903, went to Israel as a pioneer in 1923 and joined a Kibbuz. After a strenuous year he fell ill with malaria, and was compelled to move to Jerusalem. There he worked as a labourer and at the same time enrolled as one of the first students in the pre-faculty of sciences of the Hebrew University. He studied chemistry under Prof. A. Fodor, and graduated in 1928 (unofficially, since the Hebrew University was not yet recognized at the time). Being an outstanding student, he was given a study grant which enabled him to go to Brussels, where he continued his studies towards the degree of doctor of science under two distinguished teachers—Victor Henry and Jaques Errera. Despite the difficulties of a new language and environment, he completed his studies with great distinction, and was appointed an assistant. His first independent research paper was published in 1932. A year later he made the acquaintance of Chaim Weizmann, who soon recognized the high qualities of the young scientist and invited him to serve as the physical chemist of the Daniel Sieff Research Institute which was planned at the time. Thus began Hirshberg's life-long association with the Sieff and Weizmann Institutes. His scientific career can truly be called a fruitful one, as witnessed by nearly ninety research papers in various scientific journals. His well-known discovery of 'photochromism' in 1950 and the investigation of this phenomenon and of the 'photochemical memory' led by him since then, won him world-wide recognition and international acclaim.

Despite his success, he never ceased to be a 'man of the people', being on friendly terms with everybody, irrespective of grade or standing. His personality was marked by boundless devotion to his work, willingness to help, and eagerness to make a friend of whomever he met, a goal which he achieved almost always, thanks to his rich Jewish humour and his good-heartedness.

His last years were marred by great suffering because of his many maladies. Nevertheless, he put up a stubborn fight against his disease and refused to give in. He was active in the laboratory and full of plans to his last day, and succumbed to a heart attack while still wearing his white laboratory coat.

His colleagues and collaborators will always remember his high human qualities, his scientific ingenuity, and his infectious enthusiasm, and hope that the work being continued in his laboratory will serve as a living monument to him. E. FISCHER

Dr. Robert W. Lawson

ROBERT WILLIAM LAWSON, who died in hospital on November 14 in his seventy-first year, was a lecturer in the Physics Department of the University of Sheffield for thirty-six years. He went from his native town of Gateshead to Armstrong College (now King's College), Newcastle upon Tyne, in 1908 and obtained a first-class degree with honours in physics. This was followed by two years research work in the College on the production of those high-frequency oscillations which later developed into radio-waves, but the study of which was then in its infancy. This brought him an award which enabled him to go to the Radium Institute in Vienna in early 1914. He was interned on the outbreak of war but generously released on parole, so that he could continue his researches into radioactivity at the Institute. He worked long hours under difficult conditions, on an inadequate diet, and published a number of papers, particularly on the rate of emission of alpha-particles from radium. The result he obtained in this investigation was verified by later workers and is accepted as the standard value. These papers earned him the award of the degree of doctor of science of his own University of Durham. He also became one of the first Fellows of the Institute of Physics when it was founded.

On his return to Britain in 1919, Lawson was appointed a lecturer in physics at Sheffield and remained there for the rest of his life, being made a senior lecturer on the establishment of this grade. The privations he suffered in Vienna had an adverse effect on his health, and it was some time before this was sufficiently restored for him to resume experimental research. The work of teaching the influx of ex-Service students could not be deferred, however, and at once he entered on a life of service to the Physics Department. He was a lucid lecturer and it was his delight to give experimental demonstrations of his talks whenever possible. In the early nineteen-twenties he was placed in charge of the laboratories in which both the special and general degree students worked. Thus he had a large share in training the many Sheffield physicists who have attained distinction. He devised many ingenious experiments for them, some of which were shown at the open meetings of the Sheffield Physical Society which he organized between the two World Wars. He had a wide circle of friends among Continental physicists, and this, together with his proficiency in German, led to the publication of several translations of important books. Probably the most noteworthy of these was "Relativity", by Einstein, the first simple exposition of the theory which has affected science

so profoundly. His colleagues benefited from his wide reading, and in past years he was also a frequent contributor to the columns of *Nature*.

Lawson played a prominent part in the formation of the Non-Professorial Staff Association of the University and was one of its first representatives on the Senate when this recognition was accorded. He retired in 1955, but his interest in physics remained unabated. His unexpected death will be a shock to his old students, who had a high regard for him, and to his many friends. He married in 1922 and leaves a widow and daughter. J. R. CLARKE

NEWS and VIEWS

Inorganic and Structural Chemistry at Leeds: Prof. H. M. N. H. Irving

DR. H. M. N. H. IRVING has been appointed to the chair of inorganic and structural chemistry in the University of Leeds, in succession to Prof. E. G. Cox (see *Nature*, **185**, 144; 1960). Dr. Irving was born in Oxford in 1905 and educated at St. Bees School and Queen's College, Oxford, where he was a pupil of F. D. Chattaway. He took a 'first' in chemistry in 1928, a D.Phil. in 1930 and was awarded the degree of D.Sc. in 1958. He became a demonstrator in Queen's College laboratory, but when this closed down Prof. Soddy appointed him as a demonstrator in the Inorganic Chemistry Laboratory of the University. Although his early training was in the field of organic chemistry, he rapidly acquired a mastery of inorganic chemistry, and skilfully used his knowledge of organic synthesis, and familiarity with a wide range of organic substances, in an attack on various analytical problems and particularly in the application of stereochemical principles to their solution. Later he exploited solvent extraction and radiochemical methods to good effect. In these fields he has built up an international reputation. During the War he was engaged on government research problems and took an active part in local Civil Defence. He was a lecturer at St. Edmund Hall during 1935–38, and has been an official Fellow from 1938 and vice-principal since 1951. He has played an active part in the Chemical Society, Royal Institute of Chemistry and the Society for Analytical Chemistry, and has served on numerous official committees. He is the author of nearly a hundred papers on scientific subjects, and in addition to many interests outside his ordinary work he holds the licentiate of the Royal Academy of Music.

Psychological Medicine in Edinburgh: Prof. G. M. Carstairs

DR. GEORGE MORRISON CARSTAIRS, director of the Medical Research Council Unit for Research on the Epidemiology of Psychiatric Illness, Tavistock Square, London, has been appointed to the chair of psychological medicine in the University of Edinburgh in succession to the late Prof. Alexander Kennedy. Dr. Carstairs was born in India and educated at George Watson's College and the University of Edinburgh. At the University he read arts as well as medicine and was a medallist in Fine Art. He was also a well-known athlete. He served as a medical officer in the Royal Air Force in Europe and the Far East. During the War, Dr. Carstairs became interested in social anthropology, particularly in studies of the influence of different cultural environments in personality development. After the War, Dr. Carstairs held various senior appointments at mental hospitals in Edinburgh and Oxford, and also studied social anthropology as an external student of the Institute of Social Anthropology. For the next four years he held research fellowships which first took him to New York as a Commonwealth Fund Fellow, where he studied social anthropology under Dr. Margaret Mead during 1948 and 1949 in preparation for two years of field studies in Rajputana, where he carried out research while living in three primitive village communities. During part of this time he held a Rockefeller Grant and a fellowship from the Henderson Trust and worked as a graduate student of Cambridge under the direction of Prof. Meyer Fortes. His researches in Rajputana are published in his book, "The Twice Born". He has also published widely in psychiatry and in the psychiatric aspects of social anthropology.

Lister Medal of the Royal College of Surgeons: Prof. W. G. Penfield, O.M., C.M.G., F.R.S.

PROF. WILDER GRAVES PENFIELD, director of the Montreal Neurological Institute, has been awarded the Lister Medal of the Royal College of Surgeons of England, in recognition of his service to the advancement of medical and biological knowledge, especially in the fields of neurology, surgical neurology, and psychology; and equally as humane surgical healer and as scientific research worker. He will deliver the Lister Memorial Lecture in London on April 5, 1961, under the auspices of the Royal College of Surgeons of England. This is the thirteenth occasion of the award, which is made by a committee representative of the Royal Society, the Royal College of Surgeons of England, the Royal College of Surgeons in Ireland, the University of Edinburgh and the University of Glasgow.

Code of Practice against Radiation Hazards

A CODE of practice issued by the Imperial College of Science and Technology, University of London, describes the rules applicable to the use of equipment producing X-rays, to particle accelerators, and to the use of radioactive isotopes, either sealed or unsealed (Third edition, revised. Pp. v+35. London: Imperial College of Science and Technology, 1960). The code supersedes a previous one of December 1958, and deals, in the main, with administrative procedure and control; a second part consists of a number of appendixes giving detailed information and advice on practice. The purpose of the code is set out under the following headings: (1) the protection of the worker's health; the hazard includes direct radiation and the accumulation of traces of radioactive material in the body; (2) the avoidance of contamination of the laboratory; (3) to ensure the safe disposal of waste material and effluent. The code also describes the method of control, the names of referees and the health physicist, the kind of work to be registered and the procedure for registration. Conditions to be observed before work is begun are also described.

Parliamentary Secretary to the Minister for Science

In moving the second reading of the Ministers of the Crown (Parliamentary Secretaries) Bill in the House of Lords on December 8, the Minister for Science, Lord Hailsham, referred to the clause which permitted the appointment of a Parliamentary Secretary to the Minister for Science (see also *Nature*, December 3, p. 782). He said that the arrangement under which questions relating to responsibilities of the Minister for Science were answered by some six or seven different spokesmen in the House of Commons was neither popular in that House nor convenient to him. It frustrated what he thought was a main advantage in appointing a Minister for Science, namely, the production of an image of scientific policy as a consistent whole. A collection of spokesmen, however skilful, could not answer supplementary questions in the same way as someone in the Department who knew the mind of the Minister, and there was much background which could not be conveyed in the ordinary brief. He thought that the present practice prevented the building up and presentation as a whole of a coherent body of doctrine about the work of the Department. Lord Hailsham did not accept the view that the Minister for Science should necessarily be in the House of Commons. He thought there were advantages in the Minister being in the House of Lords, which might even be the ideal position; but he suggested that the Prime Minister is entitled to some latitude in this respect, and in this view Lord Alexander of Hillsborough, speaking for the Opposition, concurred.

Termites in the Humid Tropics

A symposium on "Termites in the Humid Tropics", organized jointly by Unesco and the Zoological Survey of India, was held in New Delhi during October 4–12 under the presidency of Dr. M. L. Roonwal, director of the Zoological Survey. Among the eighty-four registered participants were delegates from Burma, Ceylon, Indonesia, Pakistan and Thailand. In addition, Prof. A. E. Emerson (University of Chicago), Prof. M. S. Ghilarov (Academy of Sciences, Moscow), Prof. K. Gösswald (University of Würzburg) and W. V. Harris (Commonwealth Institute of Entomology, London) attended as guests of Unesco.

Some forty papers were submitted, the majority of which were read and discussed at one or other of the six sections—systematics and morphology, physiology and development, general biology, ecology, intestinal symbionts and termite control. Current research in India provided the basis for many of the communications. An interesting series of papers was contributed by workers at the Defence Research Laboratories, Kanpur, covering the laboratory culture of *Odontotermes* for testing purposes, the ecology of fungus gardens constructed by this genus, and the relative susceptibility of local timbers to termites. The development of the *Odontotermes redemanni* embryo was dealt with by D. Mukerji in a beautifully illustrated paper. Other communications dealt with regressive evolution among termites (A. E. Emerson), the termite fauna of the U.S.S.R. (M. S. Ghilarov), termites in relation to Indian agriculture (D. B. Reddy and T. Sankaran), a portable plant for termite-proofing timber, bamboo and thatch used for low-cost buildings (V. R. Sonti), to mention only a few. It is understood that the proceedings of the symposium will be published in due course by Unesco.

At the final plenary session a resolution was passed recommending to the consideration of Unesco the appointment of an International Termite Commission to undertake, among other things, the co-ordination of testing techniques for termite-proof materials, the study of the problem of accidental introduction of injurious termites, and the collection of information on termites as pests of growing crops and methods of control. A field excursion to the Forest Research Institute, Dehra Dun, provided a welcome break in a well-organized, but rather concentrated, programme of meetings, public lectures and broadcasts.

Trinidad and Tobago Coconut Research, Ltd.

The new Research Station situated at Champs Fleurs, Trinidad, West Indies, is an institution intended to foster research relative to coconuts. It is administered by the Directors of Trinidad and Tobago Coconut Research, Ltd., which is a non-profit making company financed jointly by West Indian Oil Industries, Ltd., Trinidad Manufacturing and Refining Co., Ltd., and the Coconut Growers' Association. The Station will be concerned with all problems pertinent to the cultivation of coconuts, with the ultimate object of increasing copra production at a decreased cost. The Station stands in the West Indian Oil Industries Compound and comprises a well-equipped laboratory, offices and stores. Relevant scientific periodicals and text-books will be collected to form the nucleus of a library to be located in the main building. The depredation of the destructive red ring disease of coconuts will compel the research team to devote most of its energies to this problem, but, as time permits, attention will be paid to other problems. It is hoped to study the insect pests of coconuts with special reference to their role as vectors of red ring disease: in this context particular attention will be paid to the coconut palm weevil (*Rhynchophorus palmarum*), and means of controlling this pest will be sought The nutrition of palms will be investigated, again in relation to red ring, but it is hoped that the results of this work will also help in the framing of general recommendations for manuring programmes. Up-to-date summaries of literature on any coconut problems which appear to be causing concern in different parts of the territory will be circulated and it is thus hoped to keep the planting community informed of the results of research into this valuable crop.

Resistant Strains of Micro-organisms

It is to be expected, and accepted, that micro-organisms inhabiting the gut of animals in the presence of antibacterial substances, such as antibiotics, will be either naturally or developmentally resistant to those substances. It is neither to be expected nor accepted that this state of affairs is necessarily undesirable or such resistant strains necessarily of enhanced pathogenicity or virulence; indeed, the evidence of animal well-being on antibiotic-supplemented diets is overwhelmingly to the contrary. However, caution is justifiable, despite the continuing lack of adverse practical or experimental data in the veterinary field, being engendered to a considerable extent by experience in human medicine with resistant *Staphylococci*; here, though, both environment and dosage-levels are very different. A recent communication in *Nature* (187, 288; 1960) described the isolation by Williams Smith and Crabb

of resistant *Staphylococci* from pigs and chickens and from their attendants; most of these organisms were resistant to 'nutritional levels' of the antibiotics fed to the animals and would be expected still to be sensitive to therapeutic dosage-levels. More recently Williams Smith (*Res. Vet. Sci.*, 1, 182; 1960) has shown that the widespread use of antibiotics in pig feeding in Britain has had no pronounced effect in increasing the number of resistant *Salmonellae* in the general pig population. This is highly significant (or insignificant?) epidemiologically, and is of particular interest in contrast with the observations of Garside, Gordon and Tucker (*Res. Vet. Sci.*, 1, 184; 1960) on experimental *Salmonella typhimurium* infection in chickens, concerning the possible effects of 'nutritionally induced' antibiotic resistance on the *Salmonella* carrier state. However, high levels of antibiotic feed supplementation were used for prolonged periods in some of their experiments, exaggerating the degree and persistence of the bacterial antibiotic resistance thus induced. Moreover, there was no evidence of any relationship between resistance, pathogenicity and virulence; it is thus important that, should problems exist, they would not relate to unduly malignant organisms of enhanced potency.

The High Polymer Research Group

The High Polymer Research Group has been founded under the chairmanship of Sir Harry Melville, for the purpose of organizing study conferences. The first conference, which will be held during April 17–20, 1961, will consider the relationship between chemical structure and physical properties of elastomers. The policy of the Group is to encourage the free exchange of ideas between active workers from all countries in the chosen field, and for that reason participation will be by invitation only. The proceedings of the Group will not be recorded, nor will papers which are read before the Group be available for publication. The offices of the Group are at 14 Belgrave Square, London, S.W.1.

Historic Books on Mining and Kindred Subjects

Recently the Science Museum, South Kensington, has staged No. 4 of its occasional exhibits of historic books on scientific and technological subjects. This new exhibition is of works on metalliferous mining, metallurgy, mining machinery, mining laws and customs, mineralogy, precious stones and related subjects (see *Nature*, 188, 538; 1960). The books themselves have been generously lent to the Museum by Mr. Robert Annan, a mining engineer, from his private collection. Many are illustrated, and nearly all are of considerable rarity. Mining is perhaps the oldest of human industries, extending back into prehistoric times, when flints were mined to make implements. Records of early mining activities before the commencement of printing are naturally very scarce, but the exhibit contains a reproduction of the illustrated title page of a fifteenth century manuscript, the "Kuttenberger Kanzionale". This is primarily a treasury of old mining songs, but contains illustrations that form a valuable record of the life and activities of a mining community of the period. The printed books cover the period from the late fifteenth to the early nineteenth century. Opportunities for the public to examine such a comprehensive collection of classic mining works occur very seldom indeed, and this exhibit should not be missed by those interested. The exhibition will remain open until December 31. An annotated catalogue has been issued, which can be obtained from the Museum, or from H.M. Stationery Office (Book Exhibitions, No. 4: Historic Books on Mining and Kindred Subjects. Pp. 32. 1*s.* 6*d.*).

Theoretical Atomic Physics in Norway

During the period covered by its second annual report (1958–59), the Nordisk Organization for Teoretisk Atomfysik was still operating on an interim basis, since the adoption of the convention on which its activities are to be based formally has had to be postponed (Pp. 46. Copenhagen: Nordisk Organization for Teoretisk Atomfysik, 1960). The temporary board, consisting of four members each from Denmark and Norway, three from Finland and Sweden, and one from Iceland, with Prof. Niels Bohr as chairman, held two meetings during the year. The staff on June 30, 1959, consisted of Prof. C. Møller as director and three scientific and three administrative staff. There were eleven Research Fellows. As in the previous year, courses of lectures and colloquia were held regularly, and detailed lists of these together with the papers published by members of Nordita are given in the report. Offprints of the papers appear as numbers in a series entitled "Nordita Publications", and are sent on request without charge to institutions and scientists interested in them. Notes of some of the lecture courses have also been issued and are similarly available.

Ergonomics and Automation

The Department of Scientific and Industrial Research has sponsored a study of the human implications of automation. This was carried out under the direction of A. T. Welford and included a critical appraisal by Miss H. M. Clay and Mr. Welford of recent research, as well as a survey of existing practice in industry by E. R. F. W. Crossman. Two publications have now been issued in the series "Problems of Progress in Industry", describing these investigations. The first, "Ergonomics of Automation", describes research relevant to the problems of the human operator in an automatic plant, with special emphasis on the design of equipment (Problems of Progress in Industry, No. 8. Pp. 60. London: H.M. Stationery Office, 1960. 3*s.* 6*d.*). The second, "Automation and Skill", gives an account of the industrial survey, and discusses the skills required of human operators in highly mechanized and automatic plants, as well as problems of selection and training (No. 9. By E. R. F. W. Crossman. Pp. 59. London: H.M. Stationery Office, 1960. 3*s.* 6*d.*).

The National Museum, Bloemfontein

The annual report of this Museum for the year ended March 31, 1960, forms encouraging reading as it records the near-completion of two new wings (Pp. 22. Bloemfontein: National Museum, 1960). This increased accommodation will give four exhibition halls and twelve extra workrooms for the staff. The latter provision will give much better facilities for research. A cafeteria has also been included. The building programme interfered with the normal activities of the Museum, and research and field work almost ceased. It has also entailed the withdrawal of the usual facilities to senior university students in anthropology and history. In spite of these additions to the buildings, exhibits illustrating the proto-bushman and fossil reptile-tracks have been prepared.

Thomas Anderson (1743/4–1812)

THE proceedings of the Scottish Society of the History of Medicine for 1959–60 is particularly interesting for the report of an address by Dr. Noel L. Poynter on the life of Thomas Anderson, the pioneer of vaccination in Scotland (Pp. 30+2 plates. Edinburgh: Scottish Society of the History of Medicine, 1960). In 1799, soon after an outbreak of cowpox in London, Anderson, "who had doubtless read the account of Jenner's *Inquiry* in Duncan's *Annals of Medicine* (12), wrote to Jenner in April asking for material to introduce vaccination in his own practice; he was able to accede immediately to his request". The excerpt from Duncan's *Annals* in the autumn of 1799 is attributed to Andrew Duncan, senior, and reads as follows: "In the village of Newhaven, in the neighbourhood of Edinburgh, many children have lately been inoculated with vaccinous matter, and they have from thence obtained complete protection against the natural disease, which then prevailed, and which still does prevail with great severity. And, indeed, from upwards of an hundred trials in Edinburgh and its environs, it has now appeared that inoculation with vaccinous matter affords equal protection against future small-pox, as inoculation with variolous matter. For these trials we are chiefly indebted to that very ingenious and able practitioner, Dr. Anderson of Leith, who was, we believe, the first to introduce vaccinous inoculation at this place, with matter which was sent him from London".

The Matjes River Rock Shelter

SOME time ago the Matjes River rock shelter was in part studied by the late Dr. Dreyer; now the excavation has been concluded by Dr. Louw as research leading to a Ph.D. degree (Researches of the National Museum, Bloemfontein. Memoir No. 1. The Museum, Bloemfontein, 1960). The result is a very competent work, and the finds have been examined in great detail. The rock shelter is in the extreme south of the African continent, roughly in the region of Plettenberg Bay. The finds include stone and bone implements, as well as skeletons. Five layers can be determined, labelled *A* to *E*. It would seem that everything found belongs to the Recent period and no trace of any true Middle Stone Age habitations occurs. The most interesting finds come from layer *C*: they recall those unearthed from the well-known Oakhurst shelter by the late Prof. Goodwin. At this time Wilton influences were penetrating into the region and mixing with the then existing folk, who would seem apparently to have been more of a Smithfield type. There are plenty of illustrations, but unfortunately they are not too good, especially those figuring the stone tools. Drawing stone implements is a specialized art, and the draughtsman must know a lot about stone knapping if a really useful illustration is to be produced. But it is excellent to gather that the study of this rock-shelter is now completed and Dreyer's beginnings brought to a conclusion. Most of the skeletons seem to be of a bushman or proto-bushman type.

Chromium in Water Supplies

THE need for research on the toxicity of chromium is emphasized in *Water Research News*, No. 9, July 1960—a periodical publication of the Water Research Association, Redhill, Surrey. In an article on "The Problem of Chromium in Water Supplies" it is pointed out that there are possibilities of chromium reaching water supplies from industrial effluents. It is generally considered that this element, particularly in its hexavalent form, is toxic, and that only very small amounts should be permitted in water supplies—less than 0·05 p.p.m. hexavalent chromium is laid down in the Drinking Water Standards of the United States Public Health Service. Methods available for removing chromium from water are costly, and the Research Association suggests that more information on the effects of chromium on living creatures is required. The available data on the concentrations toxic to various organisms are conflicting, and there appears to be no information on the mechanism of its toxic action; research on this subject would appear to be an important step in determining permissible concentrations in water supplies. Another item in this issue gives a warning that polythene joints may fail if they are brought into contact with certain active compounds, which include various oils and detergents, and are then subjected to stress. It is recommended that jointing materials should be kept away from compression fittings used for polythene, and that if possible stresses in polythene fittings should be relieved by immersion in hot water.

BIO-RAD Laboratories: Supply of Deuterium Oxide

BIO-RAD Laboratories, 32nd and Griffin Avenue, Richmond, California, have announced that deuterium oxide, a component of nuclear reactors and a key material in basic studies involving biological systems and moderation of nuclear-particle paths, will be leased for periods ranging from three months to two years at a fraction of the cost of purchasing or producing the material. The heavy water (99·8 per cent) will be on a lease/purchase basis, and can be used as the customer desires. The water is returned to BIO-RAD Laboratories when and if the customer wishes, and he will receive a credit based on the length of time water has been kept and the amount of dilution it has undergone. Plans are now being considered for similar forms of lease covering other stable isotopes including nitrogen-15 and carbon-13.

American Academy of Arts and Sciences: Grants-in-Aid

GRANTS-IN-AID, usually ranging between 500 dollars and 1,500 dollars, are available from funds administered by the American Academy of Arts and Sciences for research in any recognized scientific field, including mathematics, physical, biological and the social sciences. Applications must be received before February 1 for grants to be made in March, and before September 1 for grants to be made in October. In general, applications from individual scientists rather than from institutions are favoured, although this is not an inflexible policy. Projects dealing with explorations of the frontiers of scientific knowledge, whether interdisciplinary or within a single discipline, are preferred. Support is not usually given for work aimed primarily at fulfilling the requirements of an academic degree, or for the purchase of non-expendable laboratory equipment. Further information and requests for application forms should be addressed to: Committees on Research Funds, American Academy of Arts and Sciences, 280 Newton Street, Brookline Station, Boston 46, Massachusetts.

David Anderson-Berry Prize (1961)

A David Anderson-Berry Medal, together with a sum of money amounting to not less than £100, will be awarded in 1961 by the Council of the Royal Society of Edinburgh. The Prize will be awarded for recent work on the effects of X-rays and other forms of radiation on living tissues. Published work will be taken into consideration if submitted to the Society with the application. In addition to direct application for the Prize, proposals may be made on behalf of others. Applications and proposals should be sent to the General Secretary, Royal Society of Edinburgh, 22/24 George Street, Edinburgh 2, not later than March 31, 1961.

University News :

Edinburgh

The title of Research Fellow in the Department of Animal Genetics has been conferred on Dr. J. L. Sirlin; Mr. D. M. Weir has been appointed lecturer in the Department of Bacteriology, and Dr. R. G. S. Leask has been appointed lecturer in the Department of Clinical Chemistry.

Glasgow

Dr. J. H. Renwick has been appointed senior lecturer in human genetics. The following have been appointed lecturers: R. W. P. Drever, W. Jack and E. W. Laing (experimental and theoretical physics); I. M. Hoodless and W. Parker (chemistry); J. S. Keates (geography); and D. J. Simms (mathematics). G. L. le Bouvier has been appointed to a research fellowship in genetics, and I. Hughes and D. A. R. Wallace in mathematics. A. L. Porte has been appointed an Imperial Chemical Industries Fellow in chemistry.

The second Fleck Lecture is to be given on February 22, 1961, by Dr. John Paul (biochemistry).

For the present session, 396 new students (286 men and 110 women) have been admitted to the Science Departments, compared with 392 in 1959. The total of matriculated students in the University as a whole now stands at 6,600, compared with 6,566 in 1959.

London

Dr. D. G. Evans, director of the Department of Biological Standards in the National Institute for Medical Research, has been appointed to the University chair of bacteriology and immunology tenable at the London School of Hygiene and Tropical Medicine. Dr. J. D. N. Hill, senior lecturer in the Institute of Psychiatry and lecturer in psychological medicine at King's College Hospital Medical School, has been appointed to the University chair of psychiatry tenable at Middlesex Hospital Medical School.

Announcements

Dr. S. M. Partridge has been appointed head of the Eggs and Poultry Department of the Low Temperature Research Station, Cambridge, following the death of Dr. J. Brooks (see *Nature*, 188, 451; 1960). Dr. Partridge will also continue to be in charge of the Protein and Ion-Exchange Department.

Dr. H. E. Dadswell has been appointed chief of the Division of Forest Products of the Commonwealth Scientific and Industrial Research Organization, Australia. He succeeds Mr. S. A. Clarke, who retired in August. Dr. Dadswell, who has been with the Division since its inception, was previously assistant chief and officer-in-charge of the Division's Wood and Fibre Structure Section.

Dr. J. R. Furlong, scientific adviser since 1953 to the Pyrethrum Board of Kenya, has retired and will take charge of the London office of the African Pyrethrum Technical Information Centre in succession to Dr. T. F. West, who has been appointed editor of *Chemistry and Industry*, the journal of the Society of Chemical Industry. Dr. Furlong was chairman of the Consultative Committee on Insecticides of Vegetable Origin at the Imperial Institute, and in 1946 he took a leading part in the survey of methods for the analysis of pyrethrum, which resulted in the world-wide collaborative scheme carried out in 1948–49.

D. Van Nostrand Co., Ltd., regret to state that there are mistakes in titles of authors mentioned in their advertisement of the "International Dictionary of Applied Mathematics", published in *Nature* of December 10 (p. i of Supplement); thus Prof. B. H. Flowers, author of the section on "Nuclear Science", is now professor of theoretical physics in the University of Manchester; the section on "Aerodynamics and Hydrodynamics" is by Prof. W. A. Mair and Dr. R. S. Scorer, and that on "Probability and Statistics" by Prof. M. G. Kendall.

The Faraday Society is holding an informal discussion on "Mechanisms of the Gas-phase Reactions of the Halogens and their Compounds" in the Chemistry Department, University College, Cardiff, on March 28, 1961. Further information can be obtained from Dr. J. H. Thomas, Chemistry Department, University College, Cathays Park, Cardiff.

A symposium on "Molecular Structure and Spectroscopy" is to be held in the Department of Physics and Astronomy, Ohio State University, during June 12–16, 1961. Further information can be obtained from Prof. R. A. Oetjen, Department of Physics and Astronomy, Ohio State University, Columbus 10, Ohio.

The first international congress on "Metallic Corrosion" is to be held at the Imperial College of Science and Technology, South Kensington, London, S.W.7, during April 10–15, 1961. Further information can be obtained from the Honorary Secretary, First International Congress on Metallic Corrosion, 14 Belgrave Square, London, S.W.1.

The Mather Lecture for 1961 will be given in conjunction with the annual general meeting of the Textile Institute to be held on April 20. The Lecture will be given by Dr. A. Clow, senior producer of the Science Unit of the British Broadcasting Corporation, and his subject will be "Chemistry in Scotland and its Pioneer Contributions to Textile Technology". Further information can be obtained from the Secretary, Textile Institute, 10 Blackfriars Street, Manchester 3.

Asked for a statement on the Low Temperature Research Station, Cambridge, Mr. C. Soames, the Minister of Agriculture, Fisheries and Food, as representing the Minister for Science, in a written answer on November 24 stated that the building occupied by the Station was held on a 10-year lease from the University. The lease expired in 1966 and the University had given notice that it could not renew the lease as the space is required for other purposes. The Agricultural Research Council was considering the future of the work being carried on at the Station.

THE IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

NEW PHYSICS DEPARTMENT

IN 1953 the Government decided that, within a period of less than ten years, the size of the Imperial College of Science and Technology should be doubled. Plans were eventually prepared by the College for a massive expansion programme, involving the re-development of a large site in South Kensington, which culminated in the Jubilee scheme, announced by the College in 1957.

A significant stage in this expansion was reached on October 20, with the formal opening of the new physics building by Sir John Cockcroft. The Departments of Aeronautics and Chemical Engineering and part of the Department of Mechanical Engineering have already moved into new buildings during the past few years, but the Department of Physics is the first to be completely rehoused as part of the Jubilee scheme.

The new building has twelve floors (levels 0–11) in which the complete activities of the Department, both teaching and research, are carried out. Levels 0 and 1 are below ground-level, and levels 2–7, T-shaped in plan, rise 80 ft. above ground. Four more floors of smaller area (levels 8–11) extend the spine of the T some 50 ft. higher. The given area of 183,000 sq. ft. doubles the space provided by the old physics building, and it is interesting to note that this is provided on a site only half the size.

Teaching facilities are provided for 350–400 undergraduate students, and are confined to levels 1–4, where large corridors and several staircases make for the easy movement of large numbers of students between lecture theatres and practical laboratories. There are three lecture theatres, the largest seating 250 and the others 150 each. The former is well equipped with ciné and still projectors, and with sound equipment. In addition to its use for undergraduate courses, it has been designed in conjunction with the entrance halls and the library reading room, with a view to the holding of scientific conferences.

The main practical instruction is given in three large teaching laboratories, each of which is provided with ancillary photographic dark rooms, preparation rooms and storage space. Library facilities have been considerably extended; the book capacity is 12,000 volumes, and tables and seating for 100 persons are available day and night.

The teaching of undergraduates, concentrated on the lower floors of the building, has been further co-ordinated by the appointment of Prof. W. D. Wright, who continues also to hold the chair of technical optics, to the new post of director of undergraduate studies. He, assisted by several other members of the academic staff, will arrange the undergraduate courses and generally supervise the facilities for students in the teaching areas of the building.

Below ground-level are some very large rooms, used as research laboratories for acoustics, high-temperature physics and spectroscopy. Here, too,

Fig. 1. New Physics Department of the Imperial College of Science and Technology, London

are the students' and main workshops, used largely for the construction of research apparatus.

The main research activity, however, takes place on the upper floors of the building—levels 5–11. Although laboratories individually designed for various types of work offer advantages in the first few years to the first occupants of a new building, these are usually far outweighed by the difficulties of adapting them later for use for new people and different research. Consequently, every effort has been made to avoid the specialized design of particular rooms. Throughout the research areas an attempt has been made to provide in rooms of all sizes a uniform high standard of background amenities.

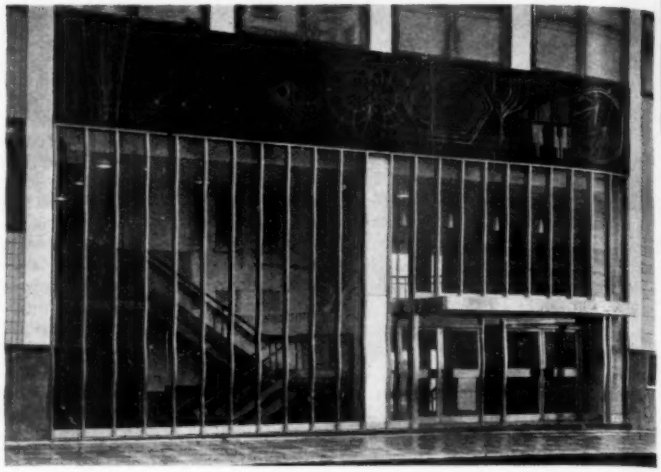

Fig. 2. Main entrance

Large, double-glazed windows provide good natural lighting, give acoustic and thermal insulation and can be blacked out completely or fitted with venetian blinds to avoid excessive glare or heating from the Sun. The building is completely ventilated with filtered air to minimize harm caused by dust on delicate apparatus and to reduce the inconvenience and cost of cleaning. Ceilings are faced with demountable acoustic tiles for quietness. These are also the source of heating, conceal some piped services and support recessed lights, so that clear plane interior surfaces are provided without restriction on the placing of apparatus. To further this flexibility in the use of rooms, recessed wall racks and concealed attachment points in the ceiling are provided for the erection of apparatus.

Electrical supplies are contained in surface-mounted aluminium wall ducts, water and gas on narrow wooden service rails. These are provided in nearly all rooms, so that even the smaller ones, which may be used as academic staff rooms or administrative offices, can equally well be used for experimental work. Practically no laboratory furniture is built-in, but is composed of standardized units which can be grouped together and, if necessary, bolted to the wall racks, according to particular needs.

The large ducts above the corridor ceilings and vertical ducts in the thickness of the corridor walls interconnect all rooms in the building. Initially these carry only those minimal supplies of electricity, water and gas for the work at present envisaged, but as new projects arise and require new supplies, readily accessible space in the ducts is available for them.

During the past five years a considerable expansion of the Department has already taken place, under great difficulties, in the old building, in preparation for the move into the new one. Physics undergraduates have increased by some 50 per cent to 315, and postgraduates by a similar proportion to about 90. Approximately 100 undergraduates from other departments also attend courses. A particular feature of the Department's development is the number of independent research groups which have been formed, each headed by its own professor. In addition to the long-standing Technical Optics Section, three more have been established in recent years: Instrument Technology, Theoretical Physics and Cloud Physics. At the same time three other professors have been appointed to assist the head of the Department, Prof. P. M. S. Blackett, in the direction of its other research activities, which now include high-energy nuclear physics, cosmic rays, electron diffraction, high-temperature physics, spectroscopy, acoustics, rock magnetism, electron physics and metal physics.

That such an active and flourishing expansion in the Department's activities should be matched with the environment and facilities of what must be one of the finest physics buildings in the world, gives promise of a great future for physics at the Imperial College.

N. C. Barford

THE NATIONAL CHEMICAL LABORATORY

THE National Chemical Laboratory held open days for visitors from industry, the universities and Government departments during October 19–21. The Laboratory's work was last on view in October 1958, shortly after the re-organization of the former Chemical Research Laboratory, so that this year's exhibition gave the first opportunity to inspect the changes and the progress made in implementing the revised research programme. Especially noteworthy, perhaps, were the increasing scope and facilities for hydrometallurgical research, and the decision to develop the earlier work on the purification and physical properties of organic compounds into a full programme of chemical thermodynamics. Although the open days showed also the progress in the Laboratory's continuing lines of research, emphasis was on newer developments.

The Extraction of Metals Group, concerned with hydrometallurgical processes and their underlying chemistry, showed its new laboratory wing, occupied

in 1959 and designed for operations on the small technical scale. Even with a relatively small scale of operation, translation of research from the laboratory bench to a technical process involves the handling of very substantial quantities of material. The new laboratory, equipped for all the main unit processes of hydrometallurgical research on a scale of up to one ton of ore per day, constitutes a very flexible and versatile adjunct to the laboratory research. Shown in operation in this laboratory was a compact solvent extraction plant embodying four stages of a recently developed rotatory-disk film contactor, which operates directly on unfiltered leach slurries. Extraction from pulps appears to be a promising technique, and the rotary contactor has already been tested over lengthy periods.

Another exhibit showed highly selective anion-exchange resins for the efficient recovery of gold from cyanide solutions. A molecular model of a segment of aminated polystyrene resin illustrated how sterically hindered functional groups, for example di-*n*-butylamino groups, can restrict the access of any but stereochemically acceptable complex ions to the exchange sites. On this basis, resins have been devised with which it is possible to achieve an exceptionally high capacity and remarkable selectivity for the linear $[Au(CN)_2]^-$ ion, at the expense of the bulkier divalent $[Zn(CN)_4]^{2-}$, $[Ni(CN)_4]^{2-}$ and other ions. Results of tests with these resins under plant conditions, in South Africa, have confirmed the promise shown in the Laboratory.

A major interest, represented by several exhibits, is the extraction of beryllium from relatively low-grade ores and concentrates. The chemical reactivity of beryllium minerals can be empirically enhanced by fusion and quenching from a high temperature; experimental methods for doing so, using induction heating and carbon tube furnaces were demonstrated. The phase changes and fundamental chemistry underlying this, and analogous molten or glassy systems, emerged from studies made by high-temperature microscopy and X-ray methods. Exhibits dealing with the solution chemistry of extraction processes made clear how relevant—and incomplete—are modern concepts of the hydrolysis and condensation reactions of aquocations and of silicic acid. Stringent health precautions are essential for work on beryllium, and methods were on view for continuously monitoring the air, in order to ensure that the beryllium concentration at no time exceeds 2 μgm./m^3.

The work of the new Chemical Thermodynamics Group has developed into one of the Laboratory's major commitments, as a long-term project well suited to a national laboratory. The exhibits showed the range of work being undertaken at Teddington, although the Laboratory is clearly still in the stage of building up some of the necessary experimental facilities. Among the important new items on show were two liquid-helium cryostats for adiabatic calorimetry down to temperatures of 10° K., in course of construction, and instrumentation for the entropy programme. In addition to its standard bomb-calorimeter the Calorimetry Laboratory showed a newly installed rotatable bomb-calorimeter; the latter is intended for heats of combustion of halogen compounds and similar materials, for which water is introduced into the bomb in order to give a properly defined end-state. Also on show for the first time was work on the computation of free energies at high temperatures from molecular spectroscopic data. Vibrational assignments for relatively complex molecules, from Raman and infra-red spectra, were exemplified by work that has been carried out on the homologous series of phenols. The Chemical Thermodynamics Group also showed its methods for determining the critical pressures, heat capacities and other relevant properties of vapours. It has made substantial contributions to the experimental techniques that are used to prepare and characterize organic compounds in extreme purity, and its apparatus for high-efficiency distillation, zone melting of organic materials, gas chromatography, etc., were also displayed.

Two main lines of investigation were shown by the Inorganic Group. Work on the separation of rare-earth elements has involved the study of different complexing agents for elution from ion-exchange columns. The resulting process has been developed to the scale of a small pilot plant, which was operating on the separation of a heavy lanthanide (holmium to lutetium) mixture. Two new topics were a continuous counter-flow process using sodium amalgam, to extract the reducible elements samarium, europium, and ytterbium from their mixtures with the non-reducible lanthanides, and the use of solvent extraction to provide a quicker and cheaper initial separation than the ion-exchange column, which is tedious and time-consuming when applied to complex mixtures. The Laboratory has also been concerned with the extreme purification of semi-conductor materials, and showed its work on the zone refining of a range of elements and on the use of radioactive tracer methods and of activation analysis for following extreme purification processes. Since not all impurities may be suitably partitioned between a crystalline element and its melt, alternative routes have been investigated, involving chemical separations or the zone-refining of suitable compounds, such as gallium trichloride, and their subsequent conversion. This extension of zone-refining to relatively fusible materials has involved the development of techniques which can be operated at subnormal temperatures.

Corrosion research has figured for a long time in the Laboratory's research programme. This year's exhibits emphasized progress in the investigation of inhibition and of microbiological corrosion. Recent electrochemical and radiochemical work, which was displayed, has shed some light on the action of chromate, benzoate and other anions that can inhibit the corrosion of iron. These ions can be adsorbed only if the potential of the iron is above the so-called 'zero charge' potential. Unless this critical potential is attained, before or after the addition of a non-oxidizing inhibitor, either as a result of aeration or by the addition of an oxidizing agent, corrosion is not inhibited.

Corrosion of metals in soils is mainly a microbiological problem involving, in the case of iron, the sulphate-reducing bacteria. From electrochemical measurements on mild steel in cultures of *Desulphovibrio* it has emerged that the corrosivity of the organisms is related to the enzyme make-up of different strains; in particular, cathodic depolarization by bacterial hydrogenase is an important factor. Corrosion-rates in soil, as compared with laboratory measurements in pure cultures, have suggested that the state of active multiplication is important, and apparatus was shown for measuring corrosion in both semi-continuous culture conditions and in batch experiments. Also on view were methods for measur-

ing the redox potential of soils as an index of their aggressiveness towards buried metals. The role of bacteria in the oxidation of inorganic materials was also illustrated elsewhere, in work on the 'natural leaching' of uranium and copper from ores. Inoculation with sulphur-oxidizing organisms, or accidental infection, markedly increases the rate of extraction of soluble sulphate, under the combined action of oxygen and water.

The Laboratory's concern with the fundamentals of gas-solid interaction, underlying corrosion, was shown also in the Director's laboratory, where work has been started on field emission microscopy as a tool for studying chemisorption and reactions on metals.

The New Materials Group, which is responsible for the bulk of the organic chemical work of the Laboratory, showed the lines of work that have emerged from the Laboratory's long-standing concern with ion-exchanging materials, and, in particular, some new materials with interesting electrochemical properties.

Several exhibits showed progress made in the development and application of ion-exchanging membranes. Of particular interest were the proton selective membranes—duplex membranes, with a layer of cation exchange material in intimate contact with a layer of anion material. The ions of water can thus move away in opposite directions from the internal interface, and the membrane is virtually permeable only to hydrogen ions. By combining such membranes with anion- and cation-permeable membranes in multi-compartment cells, possibilities arise for applying them to electrochemical processes. A five-compartment cell, used for measurements of membrane properties in the reversible conversion of sodium chloride to hydrochloric acid and caustic soda, demonstrated the behaviour of such systems.

Greater specificity in ion-exchange materials is being sought in several ways: by the synthesis of chelating polymers, by the combination of cation-exchanging membranes with complexing agents to confer selective permeability and by investigating the role of interactions between ions and polymer matrix. Work was shown on the formation of charge transfer complexes and the correlation of charge transfer interactions with selective permeability.

A new topic shown was the work on polymers with electron exchanging properties, that is, solid oxidants and reductants, capable of regeneration. The particular resins shown were based on the quinone–hydroquinone redox couple, on the redox properties of metallic atoms built into the polymer structure and on oxidants, such as chloramine-*T*. These, although not forming reversible redox systems, can be repeatedly regenerated. An interesting minor exhibit showed the contractile properties of some of these redox systems, in the form of a 'synthetic muscle' based on polyvinyl alcohol.

Also on view in the section dealing with high polymers was a method of polymer fractionation using the so-called 'gel filtration'. As applied to the elution of polymers absorbed in beads of polystyrene, it has recently been found possible, with suitably controlled and very lightly cross-linked material, to achieve a good degree of fractional elution. A rapid method may thereby be opened up for the analysis of molecular weight distributions. J. S. Anderson

SOUND PROPAGATION IN THE ATMOSPHERE

On September 8 the Acoustics Group of the Physical Society held a symposium on sound propagation in the atmosphere. The chairman was Dr. R. W. B. Stephens. Three papers were from the United States, one from Denmark and two from the United Kingdom. Two further American papers listed on the programme had to be cancelled because their authors could not get transport.

The first paper, "Recent Experiments on the Propagation of Audible Sound along the Earth's Surface", was presented by Dr. F. M. Wiener (Bolt, Beranek and Newman Inc., Cambridge, Massachusetts). Dr. Wiener gave a progress report on extensive measurements of sound propagation over land and over sea. Source and receiver heights were small, for example, 12 ft. and 5 ft. respectively, for the measurements over ground. The horizontal distances covered by the measurements were about one mile over land, and up to three miles over the sea. The dependence of the propagation on the state of the atmospheric boundary layer, 30–50 ft. thick, was stressed by Dr. Wiener and the instrumentation for measuring turbulence and the mean wind and temperature profiles up to a height of 35 ft. above the ground was described. Loudspeakers were used as the sound source. For the measurements over land, ten microphones were spaced logarithmically from the source out to a distance of 6,000 ft., and the site was flat open ground. It was shown that the measured results of excess attenuation (attenuation in excess of the attenuation to be expected from inverse square law and molecular absorption) were in fair agreement with the theoretical work of Ingard.

For the measurements over the sea, the same meteorological measurements were made as well as measurements of the distribution of particle size in sea fog using an optical method. The sound source, 40 ft. above sea-level, was placed on the shore. Captive buoys were used to mark out the microphone range and the microphones were mounted on a coast-guard ship which also carried recording equipment.

The measurements over the sea showed, in general, smaller excess attenuations than were found over land. During the experiments, which were primarily concerned with foggy conditions, temperature gradients were very small and the excess attenuations measured could be ascribed to wind-gradient effects. The trials through fog showed that, contrary to popular belief, sea fog causes little or no excess attenuation, and that any excess attenuation found under these conditions could be attributed to the wind gradient.

The second paper, "Horizontal Propagation of Sound from a Jet Engine near the Ground", by P. H. Parkin and W. E. Scholes (Building Research Station, Watford), described the third experiment in a series. This dealt with propagation from a jet engine source 6 ft. above the ground. Measurements were

made in daylight, without temperature inversions. By making measurements at regular intervals (once a week for a year) a cross-section of meteorological conditions for day-time conditions was assured. The eight microphones were spaced logarithmically from the source on a line 3,600 ft. long, and were 5 ft. above the ground. The meteorological measurements made were wind speed and direction at a height of 10 metres, the relative humidity and temperature, and wind and temperature profiles up to a height of 2,000 ft. using radio-sonde equipment.

It was shown that the propagation under the conditions of the experiment could be predicted with reasonable accuracy, say, within $\pm$ 3 db., by considering only the sign and magnitude of the mean wind component in the direction of propagation. The measurements covered the frequency-range 50–4,000 c./s., and the effect of the vector wind on the propagation varied with frequency. A marked ground effect in the region of 250 c./s. was found at all distances from the source. In this frequency-region excess attenuations of the order of 20 db. had been consistently found, even with the wind assisting propagation, under which conditions other frequencies were attenuated by less than 5 db. This effect was discussed, and it was shown that the same effect could be measured using a loudspeaker as source. The large attenuation at 250 c./s. diminished during the winter, although it was still prominent, and the authors suggested that this change may have been due to the lessening of the temperature-lapse rates at this time of the year, thus allowing the turbulence to scatter energy into this region of low-sound intensity.

In his paper, "Some Experiments on Sound Propagation in the Atmosphere", Dr. U. Ingard (Massachusetts Institute of Technology) reported on his experiments and theoretical considerations over the past few years. He stressed the difficulty found in presenting the data from experiments dealing with outdoor sound. The governing meteorological variables were not independent of each other, neither were they independent of the type of ground. The fluctuations in the received sound were discussed, and the author suggested that the peaks of the fluctuations should be considered rather than their average values, this was because his experience in the field of community reaction to noise suggested that this was subjectively the more important factor.

Laboratory experiments to investigate the propagation of pulses of high-frequency sound through a layer of turbulent air were discussed. The experiment used a statistical method of recording the pressures of the received sound, and it is evident that the effect of turbulence is to reduce the propagation of direct sound and to scatter energy into shadow zones.

Dr. Ingard described one of his large-scale outdoor experiments. A pulse of sound from a loudspeaker was followed as it travelled along the microphone range by switching between the microphones. The relative gains of the logarithmic microphone amplifiers were adjusted to compensate for the attenuation due to spherical spreading. The received sound pulses were displayed on an oscilloscope. The results of such trials confirmed the author's theoretical work on the subject, which stipulate the conditions of the wind and temperature profiles for the formation of shadow zones and the location of these zones.

The maximum attenuation in excess of the inverse square law in these shadow zones seemed to be about 30 db., as found in the previous papers, and it was stated that the scattering of energy into the shadow zone by turbulence caused this limit. The magnitude of the scattered sound increases with frequency, and so the maximum attenuation values at the high-audio frequencies are less than 30 db.

During the afternoon session, Dr. E. J. Skudrzyk (Ordnance Research Laboratory, Pennsylvania State University), presented a paper "The Fundamentals of Sound Scattering and Signal Fluctuations in an Inhomogeneous or Turbulent Medium". In his paper, Dr. Skudrzyk stated that scattering can be studied by investigating the properties of individual scatterers and by adding their sound effects. This analysis procedure leads to practically the same results as the statistical methods that are based on the correlation function. The scatterers in real media have all sizes, and are characterized by distributions such as the Kolmogorov equilibrium law of turbulence. Measurements on the distributions of the scatterers have yielded excellent verification of these laws and illustrate them with a clarity that would scarcely be attained by just studying regular turbulence. The scattering of Kolmogorov types of distributions was discussed.

"Sound Propagation in Fog" was the subject of a paper presented by Dr. R. E. H. Rasmussen (Technical High School, Copenhagen). The paper dealt at length with the history of the study of the effect of fog on the propagation of sound, and went on to discuss methods proposed for fog dissipation. Among those which had been proposed were the spraying of a saturated solution of calcium chloride and the application of heat, as in the *Fido* system during the War.

Dr. Rasmussen went on to discuss the dissipation of fog by sound waves. The mechanism of the procedure is to cause differential movement between the drops of differing sizes in the fog. This differential movement causes a proportion of the drops to collide and coalesce, the resulting larger drops tending to be precipitated.

Experiments on the dispersion of artificially created fog in a room were described. The fog density was measured photoelectrically, and the effectiveness of several sound sources in accelerating the dispersion of the fog were investigated. It was found that an air-raid siren, with an acoustic output of 100 W. at 400 c./s. accelerated the dispersion in the room by a factor of three or four.

The final paper presented to the symposium was "Wind and Temperature Results Obtained in the *Skylark* Grenade Experiments", by Dr. P. J. Bowen (University College, London). This paper described a technique for measuring wind and temperature profiles at heights up to 95 km. above the ground. The experiments are part of the British Space Research Programme and are being carried out over the rocket range at Woomera. The travel-times of sounds from the detonations of explosive charges (grenades) in the upper atmosphere were used to evaluate the wind and temperature profiles. The grenades were carried into the upper atmosphere in *Skylark* rockets, and were ejected and detonated at intervals during the ascent. An array of microphones, tuned to 15 c./s. with a bandwidth of 6 c./s., was used to record the arrival times at the ground of the signals from the detonations, while three ballistic cameras recorded the positions of the detonations. The microphones were placed up to 15 km. and the cameras up to 60 km. from the launch site. An inde-

pendent measurement of wind speed was made, using metal strips ejected from the rocket and tracking them with radar.

Results were shown of wind and temperature profiles up to a height of 95 km. above the ground. Radio-sonde ascents provided the data for the first 30 km. The agreements in the region of overlap between the sonde data and the data from the grenade experiments were good, of the order of 2 metres per sec. for the wind-speed and 2° C. for the temperature. Similar agreement was found between wind-speeds measured by the grenade experiment and by the radar tracking of the metal strips.

W. E. Scholes

SCIENCE IN GRAMMAR SCHOOLS

A BOOKLET, "The Provision and Maintenance of Laboratories in Grammar Schools (1959)", reports the results of a survey on science in grammar schools conducted by means of a questionnaire issued by a number of teachers' organizations during 1959*. The booklet reveals some improvements following an earlier survey in 1957, but shows that many critical difficulties still remain.

Replies were analysed from 694 grammar schools, widely distributed over England and Wales, and totalling, between them, 374,000 pupils. Analysis revealed that, generally speaking, boys' and mixed schools were better provided with facilities for science than girls' schools.

91·4 per cent of the pupils took science, compared with 90·9 per cent in 1957. During the first three years almost all pupils do some science. In the fifth year, when the examination for the Ordinary Level, General Certificate of Education, is usually taken, about 90 per cent of the pupils are taking science. In the sixth form, in girls' schools, the proportion studying science—including those who are not specializing in it—can be as low as 46 per cent, and in boys' schools as low as 66 per cent. When the sixth formers who are specializing in science are examined in girls' schools, the number of pupils is less than half that in the boys' schools (which is about 60 per cent); in mixed schools the position is somewhat in between.

Between 1957 and 1959 there was a small increase in the size of sixth-forms. Nevertheless, statistics showing the average size of the science sixth-forms of smaller girls' and mixed schools suggest that some schools still have uneconomically small sixth-forms.

Boys' schools tend to concentrate on physics and chemistry, and girls' schools on biology. General science has lost further ground, being a bad fourth after the three individual subjects. From a total of 13,626 pupils whose science subjects were examined, physics had established itself as the most widely taken subject with 10,619 sixth-formers. Next comes chemistry with 8,603, biology with 2,091, zoology with 1,987, botany with 1,430 and geology with 146.

Only 45 per cent of 547 local education authority schools have laboratory provision in accordance with Ministry of Education recommendations, compared with 44 per cent in 1957. Throughout England and Wales the number of new laboratories and laboratories commenced during 1958–59 totals 486 in these schools. Permission has been given for the future building of 482 more laboratories. Even when this work is completed, the laboratory position in local education authority grammar schools will still fall far short of that in direct grant and independent schools.

Direct grant and independent boys' schools have increased their provision of laboratory assistance since 1957, but the position for the local education authority schools, as shown in the sample 568 examined, indicates a slight regression. By using standards of laboratory space recommended by the Ministry, and the number of technicians per number of laboratories considered necessary by the Science Masters' Association, only 10 per cent of local education authority grammar schools can be said to be satisfactorily provided with laboratory assistance.

The following table shows the amounts spent per annum for each pupil taking science, averaged for schools of stated types:

Total No. of schools in sample	Type of school	Boys	Girls	Mixed
578	Local Education Authority Grammar	12*s.* 3*d.*	8*s.* 8*d.*	10*s.* 10*d.*
54	Direct grant	21*s.* 11*d.*	8*s.* 3*d.*	—
43	Independent	27*s.* 1*d.*	9*s.* 8*d.*	—
12	Comprehensive	—	—	4*s.* 9*d.*

Additional problems mentioned by the greatest number of schools are as follows: lack of science staff (124 schools); very large classes (197); staff not appropriately qualified (72); more laboratory stewards needed (68); sixth-form accommodation inadequate (46); practical work very limited (31).

* Science Masters' Association. Pp. 16. (London: John Murray; published for the Science Masters' Association, 1960.) 1*s.* net.

STATISTICS ON SPECIAL EDUCATION

THE term 'special education' has been used in educational literature to refer to the "education of pupils who deviate so far physically, mentally, emotionally, or socially from the relatively homogeneous groups of so-called 'normal' pupils that the standard curriculum is not suitable for their educational needs; involves the modification of the standard curriculum in content, methods of instruction, and the expected rate of progress to provide optimum educational opportunity for such pupils; carried on in special classes, in special curricula, or special schools".

In the first Unesco questionnaire on educational organization and statistics, distributed in 1949,

data under 'special education' were requested covering "institutions of a specialized nature intended for children handicapped physically, mentally and morally". Continued experience of gathering educational statistics and of dealing with problems connected with international statistical comparisons led to various specifications of the term, from the recommendation of the first Expert Committee on Standardization of Educational Statistics in 1951 to classify "all general or vocational education given to physically or mentally handicapped socially maladjusted, retarded or backward persons" as "Special education", to the recommendation concerning the international standardization of educational statistics adopted by the general conference of Unesco at its tenth session, held in Paris in December 1958. This asked that statistics be presented on "Special Education, covering all general or vocational education given to children who are physically handicapped, mentally handicapped, socially maladjusted or are in other special categories".

Unesco's only statistical questionnaire devoted to the special education of handicapped and other atypical children was sent out at the end of 1953. The term 'special education' was "to cover the training whether in special schools or in special classes in the regular schools of the country, of children who: (1) require special provision for predominantly mental, or psychological, disability; (2) require special provision for predominantly physical disability; (3) have no fixed home; (4) are in correctional institutions".

The next Unesco collection of statistics on the education of atypical children was made when a general questionnaire on all levels of education was sent out in 1955. It was stated that "special education covers pre-school, primary and secondary schools for mentally handicapped children, for physically handicapped children; for delinquent children". It also covers special classes for similar groups of children in regular schools.

The replies to these questionnaires showed considerable variation as to both schools and classes. A few countries considered the education of highly intelligent children to be part of special education (for example, Australia, Canada, the United States of America). A smaller number of countries (for example, Belgium and the Netherlands) considered education of itinerant children as part of special education. Schools for juvenile delinquents and schools for abandoned or neglected children were sometimes included, sometimes not included.

In the latest report, all those types of education have been included, in a particular country, as part of 'special education' of atypical children*. When possible, schools which were not considered in the particular country as providing special education, but which were so considered in other countries and which had certain features that marked them off notably from other schools providing courses at a similar level, were also included. In practice, these schools were most often schools for delinquent children. On the other hand, no attempt was made to include courses of correspondence education, although they have often been used for instruction of handicapped children.

Certain institutions the function of which is not principally educational—homes for children, observation centres—have been included on occasion, usually because in the country itself the institution was considered as having a special educational role.

Statistical tables, arranged on a country-by-country basis, are presented for 53 countries. For certain other countries little information was available, and is included separately.

* UNESCO. Statistics on Special Education. (Statistical Reports and Studies.) Pp. 154. (Paris: UNESCO; London: H.M. Stationery Office.) 7 NF.; 10s.; 2 dollars.

RECRUITMENT TO THE CIVIL SERVICE

THE ninety-fourth report of the Civil Service Commissioners*, covering the year April 1, 1959–March 31, 1960, in which Sir Frederick Brundrett succeeded Sir Charles Snow as scientific adviser on the latter's resignation, notes some signs of improvement in recruitment to the Administrative Class. The results of the competitions for posts in Branch *A* of the Foreign Service were also much better than recently, and after filling the advertised vacancies there was a small surplus of acceptable candidates available to help make good shortages in past recruitment. Nevertheless, both the Administrative Class of the Home Civil Service and the Senior Branch of the Foreign Service need to recruit directly a larger number of men and women than has been possible recently, and the upper age limit for entry to the open competitions for these classes is being raised from 24 to 28 in 1961, and also for the related competitions for the Special Departmental Classes.

The most important feature of the year, however, was the continued difficulty in recruitment to the scientific, professional and technical classes. For some years the Commissioners have failed to fill an adequate proportion of the vacancies notified in the scientific classes, especially in the scientific officer grade. During 1959–60 the situation has worsened and the Commissioners regard the present situation with grave disquiet. The number of applications in open competitions for nearly all the scientific classes increased, but the average quality of these candidates, especially for the scientific officer and senior scientific officer grades, has noticeably deteriorated. In spite of a small increase in the number of applications in the senior scientific officer grade and in the number recruited, namely, 70, little more than half the 115 vacancies were filled; and in the scientific officer grade only 60 were recruited to fill 380 vacancies. The shortages are mainly among physicists, engineers, chemists and mathematicians.

There was a slight increase in the number of candidates for the experimental officer/assistant experimental officer grades, but the number who were successful remained steady, and only 102 out of 117 vacancies in the former and 297 out of 404 in the latter class were filled. The number of applications for the assistant (scientific) class decreased

* Report of Her Majesty's Civil Service Commissioners for the period 1st April, 1959, to 31st March, 1960. (94th Report.) Pp. 39. (London: H.M. Stationery Office, 1960.) 2s. 6d. net.

considerably and the number of candidates successful fell by a third; only 305 out of 978 vacancies were filled, but the balance of departmental needs is met largely by the employment of temporary assistants (scientific), who may thus acquire the period of experience necessary to qualify for establishment by competition.

Difficulty continued in the recruitment of patent examiners, and only 17 out of at least 65 vacancies were filled. Only for scientific research fellowships was the situation improved, the number of candidates being up by 50 per cent and the number of fellowships awarded, namely, 27, was nearly doubled. Sixty-eight candidates for research fellowship or scientific officer posts were interviewed in April 1959 in Washington, Ottawa and New York, in a joint recruiting effort with the Atomic Energy Authority, and as a result 5 research Fellows, 4 senior scientific officers and 2 scientific officers have taken up duty in the Scientific Civil Service. The number of candidates similarly interviewed during 1960 was more than doubled.

The general situation in the Works Group of the Professional Classes was largely unchanged; the number of vacancies tended to increase, but the number of candidates was stationary or in some fields tended to decrease. The major shortages are still in civil engineers, quantity surveyors and certain classes of mechanical and electrical engineers, particularly electronics specialists. The Commissioners were concerned with the filling of senior professional posts in the new Inspectorate of Nuclear Installations set up by the Minister of Power, and although unable to fill some of the more specialized posts, they were impressed by the high proportion of applicants who could already claim good experience in nuclear engineering. The Commissioners have still to meet the increase in the demand for architects caused by the formation of the War Department Works Directorate, and in the Technical and Drawing Office Classes there are shortages corresponding to those in the professional grade; candidates coming mainly from within the Service. A shortage of good candidates in the competition for psychologists is also noted, as well as difficulty in attracting good candidates for posts as librarians in Government departments: 12 out of 23 such posts were unfilled.

TELEVISION AND ADULTS

TO Dr. Hilde Himmelweit's inquiry into the effects of television on children is now added the report of an investigation into the way television has affected family life*. This inquiry was directed by Dr. W. A. Belson and carried out by the Audience Research Department of the B.B.C. As is indicated by Prof. M. G. Kendall in an accompanying note, the report can be regarded as providing a reliable account of the effects of television on families.

How television affects family life is described in a number of ways. Families spend more time at home, particularly during evening transmissions, but there is a tendency also for viewers to make up for this by going out more when television is not on. There is some evidence of variation in this pattern according to the area and the season, but there is nothing to suggest that these changes are only temporary. One kind of family, however, the large family, is exceptional. Television has not increased the degree to which members of bigger families stay together at home: on the evidence of three of the four surveys which were carried out in London, Birmingham and Wakefield at different seasons of the year, television appears in this case to have had the reverse effect.

All four surveys reveal the effect of television to have been to increase the degree to which the married couple stays at home together in the evening period, especially in Wakefield. During the rest of the day the effect varies markedly from survey to survey, couples in some areas going out more after they have acquired television sets. Television's effect in keeping the couple at home together varies with the age of the set, but the particular pattern of change is not the same in each survey.

The effect also varies according to the type of family from which the couple is drawn, those from the 'larger families' tending now to spend less time together. The effect of television in keeping them together at home is greater when both are employed than when only one is employed.

Of the effects of television in keeping children and young people at home, the most that can be said is that on balance television tends to result in children and young people spending more time in the home—but not much more. Television's effect on home-centred activity is either small or negligible. This applies also to the diversity of range of home-centred activity, though the evidence does not rule out shifts in the 'kinds' of activities pursued.

There are distinct differences in the effect of television according to the length of set ownership. While the year-by-year pattern of change in the four surveys differs quite a lot, these patterns exhibit some common tendency to return towards the level of pre-television after about five years. This tendency, however, is neither strong nor undeviating and it may set in after either an earlier increase or an earlier decline. In London, both in summer and winter, and in Birmingham, in winter, television has led to a small reduction in the total amount of joint activity occurring in the home. In summer in Wakefield it increased to a limited extent.

In the early stages of ownership, television may lead to either an increase or a decrease in the joint activity in the home, depending on the survey area or the season. But there is a long-term tendency for the amount of joint activity to return towards the level before television.

Dr. Belson and his colleagues also examined the effects of television on visiting and entertainment. There is an increase, in all four surveys, in the number of guests in viewer households during the average half-hour of the day. The increase is moderate in London in the summer, large in the winter, and large also in Birmingham and Wakefield. The amount of the change varies by time of day, the main

* Television and the Family. (A Report on an Enquiry designed and directed by Dr. W. A. Belson, and carried out by the Audience Research Dept. of the B.B.C. under the supervision of Professors A. R. Knight, M. G. Kendall, P. E. Vernon and Barbara Wootton.) Pp. xx+151. (London: British Broadcasting Corporation, 1959.)

increase being in the afternoon and evening periods. At its maximum, which is during evening transmission time, the increase is very large, and in some surveys it almost doubles the number of visitors present.

Some of the visitors to viewer homes come as expected guests while others 'drop in' casually. With formal or 'expected' visiting, there is an increase in all four surveys, particularly those dealing with winter behaviour. With casual visiting, however, the increase is limited mainly to London (winter), some of the other surveys producing evidence even of slight reduction. There is a lot of variation in the effect of television according to the length of set ownership, but only with casual visiting is there any consistent trend; in this case it suggests a return towards pre-television level.

The investigators are to be commended not only for the clarity of their report but also for the way they have demonstrated the validity of their findings.

UNGULATES OF THE PARC NATIONAL ALBERT

A PAPER reporting the results of a study of the ecology of the twenty-two species of ungulates living in the Albert National Park in the eastern (Belgian) Congo, carried out from July 1957 to December 1959, forms fascicule 1 of the "Exploration du Parc National Albert" published by the Institut des Parcs Nationaux du Congo Belge ("Introduction a l'Ecologie des Ongulés du Parc National Albert", par F. Bourlière et J. Verschuren. Bruxelles, 1960). The report gives a full description of the various habitats that can be found in the 8,090 sq. km. of the Park, with emphasis on their geographical, climatic, edaphic and botanical characters, and compares their present state with photographic records of thirty years ago. On the whole there has been no great change, the loss of tree cover in some places being compensated by increases elsewhere. A detailed consideration is given to the geographical distribution of the various species of ungulates (and the elephant) with special attention to their autoecology and food habits. Although many species are plentiful, three—the elephant, hippopotamus, and buffalo—are the dominant species, and there is some evidence from a few marked animals that individuals tend to be surprisingly restricted to their territories.

Studies on the density of the ungulate populations were made by regular censuses, and population structure and dynamics are dealt with in separate chapters. During the past thirty years the population of different species has varied in different ways in the same environments. Elephants have increased by immigration, the numbers of hippopotamuses have remained stable, and despite epidemics of rinderpest there has been a spectacular increase in the buffalo population. Other species, such as the topi and the Uganda cob, have increased again after reaching a low level about 1940. Apart from epidemics of rinderpest affecting buffalo, and of anthrax affecting hippopotamus, a number of animals are frequently killed by lethal concentrations of carbon dioxide of volcanic origin. Competition for food in the various environments does not appear to play an important part among the ungulates of the Park.

The authors conclude that on the whole the open plains of the Albert National Park harbour the highest ungulate biomass ever found in Africa. Nevertheless, with the exception of the elephant, the species do not seem to exceed the carrying capacity of the environment. The report is illustrated with forty-nine plates of excellent and well-chosen photographs.

IODIZED SALT AND ENDEMIC GOITRE

THE September issue of *The Chronicle of the World Health Organization* is devoted to endemic goitre (14, No. 9; September 1960). The importance of iodized salt as a means of control is well brought out, as are the problems of instituting programmes of mass prophylaxis because of difficulties in manufacturing suitable grades of iodized salt.

Inexpensive and comparatively simple processes are now available which are applicable to any of the usual methods of salt manufacture and give products stable under exacting climatic conditions. Besides descriptions of the manufacturing methods, optimum dosages of iodized salt for individuals in different areas are reviewed.

The optimum level of iodization of salt depends on the average daily dose of iodine needed to prevent goitre in a community and on the average daily consumption of iodized salt per head. The available evidence suggests that, in endemic goitre areas, each person should receive a daily supplement of about 150 μgm. of iodine. In some areas, larger supplements (up to 300–400 μgm. daily) appear to be necessary, presumably in order to counteract the effect of goitrogenic agents. The consumption per head of salt varies with racial, climatic and other factors; it is higher, for example, in tropical than in temperate climates. It is also necessary to take into account whether all food salt is to be iodized, including that used by food industries, or only table salt.

In the United States, Canada and most countries of Latin America, the level of iodization is based on an estimated average consumption of 6·5 gm. per head of table-salt each day, and is calculated to provide a daily supplement of 500 μgm. of iodine, or 650 μgm. of potassium iodide. The level is thus 1 : 10,000. In most European countries, much lower levels are used, calculated to supply only the 100–150 μgm. of iodine per day estimated to be the body's actual physiological requirements. Thus, in Switzerland, where all food salt is iodized, the level is 1 : 100,000, while in the United Kingdom, where only table salt is iodized, the level is 1 : 40,000. Holman and McCartney suggest that, for countries with a moderate goitre-rate, the most satisfactory level is

probably 1 part potassium iodide to 20,000 parts of table salt, the level at present adopted in New Zealand. In countries with a high prevalence, the level of iodization should be increased to 1 : 10,000. In all events, the level fixed by the public health authorities should ensure that a minimum of 150 μgm. of iodine is available in the quantity of salt consumed daily per head, and where the dietary standard is low or there are other adverse factors, this amount should be increased to 300–400 μgm.

It is important to ensure not only that the salt has the required iodine content when it leaves the factory but also that no loss of iodine occurs in storage.

BRADYKININ

Synthetic Bradykinin : its Biological Identity with Natural Pure Trypsin Bradykinin

ABOUT twelve years after its discovery by Rocha e Silva, Beraldo and Rosenfeld[1] bradykinin was isolated, synthesized and its structure elucidated.

Rocha e Silva *et al.* first succeeded in preparing a strongly enriched preparation of bradykinin[2]. The next steps were due to Elliott, Lewis and Horton : the isolation of pure natural trypsin bradykinin[3], the description of the pharmacological activity of the pure substance[4] and, after degradation studies, proposal of a structure (Arg-Pro-Pro-Gly-Phe-Ser-Phe-Arg)[5]. Synthesis of the above-mentioned octapeptide yielded a compound which was practically inactive[6–10]. It was concluded that the proposed structure was incorrect. Other polypeptides containing the amino-acids of pure natural bradykinin were therefore systematically synthesized[7,11] and biologically tested[7,8] in our Laboratories. An octapeptide with a slightly different amino-acid sequence H-L-Arg-L-Pro-Gly-L-Phe-L-Ser-L-Pro-L-Phe-L-Arg-OH was found to possess bradykinin-like activity, but to a lesser degree[7,8]. This prompted Boissonnas, Guttmann and Jaquenoud to synthesize a nonapeptide H-L-Arg-L-Pro-L-Pro-Gly-L-Phe-L-Ser-L-Pro-L-Phe-L-Arg-OH[7,8,11], which in its biological activity and in its chemical, biochemical and biophysical properties was indistinguishable from natural bradykinin. We therefore stated[7,8] that this nonapeptide was identical with bradykinin or closely related to it.

Having been informed of these results in a personal communication, Elliott *et al.* carried out new degradation studies and were able to prove that natural bradykinin has, in fact, the same structure as the synthetic nonapeptide[12].

The present investigation, a direct comparison of the synthetic nonapeptide with pure trypsin bradykinin, was undertaken to furnish further evidence that the two substances are identical.

Natural trypsin bradykinin (a sample of 100 μgm. with an activity of 80 μgm., which does not contain other biologically active peptide impurities, kindly supplied by Dr. Lewis) and synthetic nonapeptide as trifluoracetate were compared for effect on isolated guinea pig ileum (Tyrode, 10 ml. bath, 37° ; 4-point assay), isolated rat uterus (de Jalon, 10 ml. bath, 30° ; animals pretreated with 0·2 mgm. stilbœstrol, subcutaneous ; 4-point assay), blood pressure of the rabbit (1·6 gm./kgm. urethane subcutaneous ; 4-point assay) and on capillary permeability in the guinea pig (0·1 ml. of test solutions intracutaneously, animals pretreated with intravenous Evan's blue, for details see ref. 7). The results are given in Table 1.

Table 1. Comparative Evaluation of Biological Activity of Synthetic and Natural Bradykinin

Test	Synthetic nonapeptide	Natural trypsin bradykinin
Isolated guinea pig ileum (mean of 11 exps.: each comprising 4 groups of 4 points ± *S.D.*)	98 ± 7 per cent	100 per cent
Isolated rat uterus (mean of 9 exps. : each comprising 4 to 6 groups of 4 points ± *S.D.*)	95 ± 5 per cent	100 per cent
Rabbit blood pressure (mean of 4 exps. : each comprising 2 to 4 groups of 4 points ± *S.D.*)	89 ± 13 per cent	100 per cent
Capillary permeability, guinea pig (results from 16 animals)	10 ngm./0·1 ml. 12 × = 3 × > 1 × < 1 ngm./0·1 ml. 11 × = 4 × > 1 × < 0·1 ngm./0·1 ml. effects in 9 of 16	10 ngm./0·1 ml. 12 × = 3 × ≤ 1 × > 1 ngm./0·1 ml. 11 × = 4 × ≤ 1 × > 0·1 ngm./0·1 ml. effects in 9 of 16

It can be seen from Table 1 that within the limits of the assay methods employed there is no difference between the activity of the synthetic nonapeptide and trypsin bradykinin. We therefore conclude that our synthetic nonapeptide is identical with trypsin bradykinin.

The recent developments in bradykinin research present a rather unusual situation, since this naturally occurring potent polypeptide was synthesized[7,8,11] before the complete structure of bradykinin was known.

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Natural and Synthetic Bradykinin

SINCE the isolation of natural bradykinin by Elliott, Lewis and Horton[1], a nonapeptide has been synthesized[2,3] and its structure agrees with that proposed[4] for the natural product. The structure is as follows: Arg.Pro.Pro.Gly.Phe.Ser.Pro.Phe.Arg.

The reported pharmacological properties of the synthetic bradykinin[5,6] appeared to be similar to those found with the natural product[7]. However, in order to establish the fact that the synthetic and the natural substances are the same, it was necessary to make a direct quantitative comparison of their pharmacological actions.

Table 1. RATIO OF ACTIVITY OF NATURAL TO SYNTHETIC BRADYKININ

Biological activity and preparation	Natural/synthetic
Smooth muscle contracting activity	
Guinea pig ileum	1·0, 0·8, 1·0, **1·1**
Rabbit duodenum	0·6, 0·8, **1·0**
Rat uterus	1·4, 0·6, 1·0, **1·0**
Smooth muscle relaxing activity	
Rat duodenum	0·8, 1·4, 1·1, **0·9**
Rat colon	1·4, 0·7, 0·8, **0·8**
Vasodilator activity	
Human forearm*	0·7, 1·0
Cat hind limb	1·0, 1·0, 0·9, **1·0**
Depressor activity	
Cat blood pressure	1·0, 0·8, **0·9**
Increased capillary permeability	
Guinea pig skin	1·0, 1·0, 0·9, 1·0, **1·0, 0·9**
Rabbit skin	1·1, 1·0, 0·9, 1·0, **0·9, 0·8**
Pain production	
Human blister base†	1·0, 1·0, 1·0, **1·0**

Each numeral represents the result of one experiment. The numerals in bold type are the result of comparison with synthetic bradykinin made by Parke, Davis (which was 80 per cent pure), the remainder with that made by Sandoz (which contained 35 μgm./ml.).

* From Fox, Goldsmith, Kidd and Lewis (ref. 8).

† This test was sufficiently accurate only to establish that the threshold dose of each sample was of the same order, that is, 10^{-7} gm./l.

The pure natural bradykinin of Elliott *et al.* was compared with two samples of synthetic bradykinin—one made by Sandoz, Ltd., and the other by Parke, Davis and Co.—on eleven different biological preparations. In Table 1, the ratio of natural bradykinin to synthetic bradykinin is given for the activity on these eleven preparations, and in Fig. 1 the method of obtaining these ratios is illustrated for the vasodilator activity by comparing the responses to a range of doses varying between 0·5 μgm. and 0·02 μgm.

Within the limits of experimental error the sensitivity of all eleven preparations to both natural and synthetic bradykinin was the same, proving that the natural and the synthetic bradykinin are identical.

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Direct Comparisons of the Synthetic Nonapeptide with Trypsin Bradykinin

IN April 1960, Elliott, Lewis and Horton[1] proposed an octapeptide structure for bradykinin. This was synthesized and found inactive by three independent groups of workers[2–4]. After discussion between Boissonnas and Elliott[5], Boissonnas, Guttmann, Jaquenoud, Konzett and Stürmer[2] described the nonapeptide L-arginyl-L-prolyl-L-prolyl-glycyl-L-phenylalanyl-L-seryl-L-prolyl-L-phenylalanyl-L-arginine, with properties resembling those of bradykinin. Elliott, Lewis and Horton[5] have concluded on chemical grounds that trypsin bradykinin has the structure of this nonapeptide, and Konzett and Boissonnas[6] have recently published biological evidence supporting the view that this peptide is identical with bradykinin.

The present work aimed at comparing directly on several biological preparations the synthetic nonapeptide with bradykinin to provide further evidence bearing on the question whether the two substances are identical. We used a specimen of the nonapeptide synthesized by Nicolaides and De Wald[7] and specimens of highly purified trypsin bradykinin (85 and 30 per cent pure) prepared by Elliott, Lewis and Horton[8]. In comparisons on the guinea pig ileum we also used a crude isolate of bradykinin (0·05 per cent pure) prepared by Lockhart and Jones[9] by

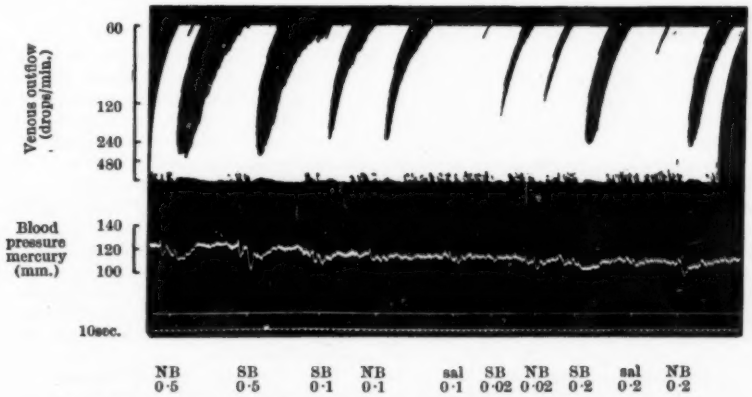

Fig. 1. Cat, 2·5 kgm. anæsthetized with chloralose 60 mgm./kgm. Upper tracing record of venous outflow from the hind limb. Lower tracing arterial blood pressure. Close arterial injections of natural bradykinin (NB) and synthetic bradykinin (SB), 0·5, 0·1, 0·02 and 0·2 μgm., and of saline (sal) 0·1 ml. and 0·2 ml. Comparison of the dose-response curves in this experiment gave a ratio of 1·0

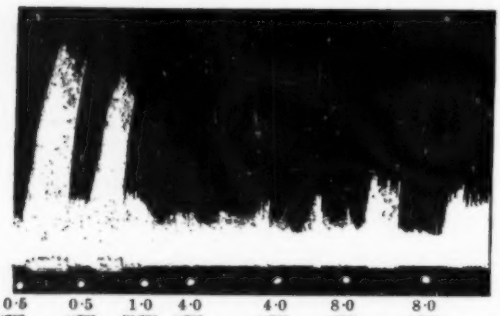

Fig. 1. Guinea pig lungs *in vivo*. Bronchoconstrictor responses to nonapeptide (N) and 85 per cent pure bradykinin (B) and their suppression by calcium acetylsalicylate (CaA). Substances administered intravenously. The guinea pig weighed 580 gm.

the action of crystalline trypsin on heated bovine serum globulin and previously standardized against pure bradykinin. The results (Table 1) show no significant difference between relative potencies of nonapeptide and trypsin bradykinin on the three preparations. This specimen of nonapeptide appeared to contain roughly 70–90 per cent active substance.

On the guinea pig lungs *in vivo*, both nonapeptide and bradykinin caused bronchoconstriction (Fig. 1), which was suppressed by calcium acetylsalicylate[10] (2 mgm./kgm., intravenous). Larger doses of nonapeptide or of bradykinin overcame this suppression.

The foregoing evidence supports the view that L-arginyl-L-prolyl-L-prolyl-glycyl-L-phenylalanyl-L-seryl-L-prolyl-L-phenylalanyl-L-arginine is identical with bradykinin prepared by the action of trypsin on bovine serum.

Table 1. Comparative Potencies of Nonapeptide and Trypsin Bradykinin on three Biological Preparations

Biological preparation	Reference specimen of bradykinin (percentage purity)	Potency of nonapeptide in terms of pure bradykinin	95 per cent fiducial limits
Guinea pig ileum	85	0·75	0·58–0·94
		0·67	0·54–0·78
	30	0·68	0·64–0·72
	0·05	0·86	0·79–0·94
		0·85	0·79–0·92
		0·90	0·82–1·02
Rabbit blood pressure	85	0·71	0·49–0·94
	30	0·56	0·39–0·78
Rat uterus	85	0·86	0·76–0·99

We thank Dr. Warner for statistical analyses.

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MEMBRANOUS CYTOPLASMIC GRANULES IN INFANTILE AMAUROTIC IDIOCY

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INFANTILE amaurotic idiocy is characterized chemically by an accumulation of gangliosides in the nervous system. It has been suggested that the gangliosides occur naturally in polymeric form and in association with polypeptides or proteins[1]. The appearance of the involved neurons and results of histochemical investigations of this disease suggest that the ganglioside increase takes place within neurons and in some of their processes[2]. In two chemically confirmed cases of infantile amaurotic idiocy, examination of neural tissue by the electron microscope revealed structures unique to this lipidosis and of theoretical importance. We are presenting the morphology of case 1 as illustrative and the analytical findings of both cases as supporting the clinical and histological diagnosis of infantile amaurotic idiocy as well as for their bearing on the morphological findings.

In case 1 the neurons within the central nervous system were everywhere distended and rounded. The few remaining Nissl granules were grouped about the nucleus, which was usually peripherally located. In paraffin-embedded material the neuronal cytoplasm contained fine granules loosely packed in the largest cells and densely arranged in the smaller cells. This material in the most distended cells was very faintly positive in preparations stained with periodic acid–Schiff but more strongly positive in the dense neurons. The neuronal contents stained very pale yellow with sudan IV. They were strongly positive when stained by the iron hæmatoxylin method of Spielmeyer and Kultschitsky. Macrophages in the molecular layer, the white matter, and necrotic zones contained large amounts of fat stained brick red with sudan IV. Large reactive astrocytes were very prominent throughout. Severe neuronal loss was seen in the cerebellar granular layer. Myelin was best preserved in the corpus callosum, around the dentate nucleus and in the striate bundles of the basal ganglia. There was no particular sparing of subcortical association fibres.

The tissue fixed with formalin was treated with Palade's solution of veronal acetate buffered osmium tetroxide, embedded in methacrylate, sectioned on the Porter–Blum microtome and examined in a Siemens Elmiskop 1. The tissue was poorly preserved

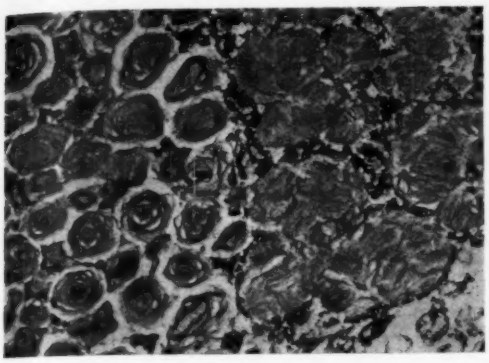

Fig. 1. Close-packed cytoplasmic granules of both types (× *c.* 9,700)

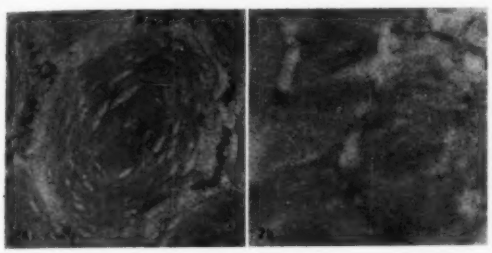

Fig. 2. *a*, concentric or spiral types of intraneuronal granule (× *c.* 12,000). *b*, cytoplasmic granule of type with flat lamellæ (× *c.* 27,000)

because it was a post-mortem specimen and had been previously fixed in acidic formalin. However, there were membranous granules measuring 0·5–2·0μ in diameter very strikingly prominent in the neuronal cytoplasm (Fig. 1). These were of two general types. The more common was a sphere made up of spiral or concentrically layered membranes which were arranged in pairs of osmophilic lines separated by a clear zone (Fig. 2). The lines and the clear zone each measured about 25 Å. The membrane pairs were irregularly arranged and separated from each other. The second type of granule was ovoid and bounded by a paired membrane which enclosed close-packed, flat, paired lamellæ. The membrane spacings were similar to those of the first type. Compound type granules with a concentric periphery and central flat lamellæ were seen occasionally.

Membranous granules with similar characteristics were found in the second chemically confirmed case where the tissue was frozen immediately subsequent to autopsy. In a third case of infantile amaurotic idiocy cortical tissue fractions obtained by gradient centrifugation also contained these granules in a good state of preservation.

For determination of lipid constituents brain tissue of both cases was treated by the procedure of Folch[3]. This resulted in a chloroform lipid-rich phase, an aqueous phase containing gangliosides and water-soluble small molecules, and an insoluble residue, largely denatured protein, which was removed by filtration. The aqueous phase was dialysed extensively. In addition to the usual determinations for lipids in the chloroform phase, the phospholipids were identified chromatographically[4]. The gangliosides were estimated in the aqueous phase by sialic acid-dependent methods[5,6]. Amino sugars in the aqueous and lipid phases were determined following hydrolysis[7] and separation on a 'Dowex' column[8]. The neutral sugars of the aqueous hydrolysate likewise were estimated following this separation and all the sugar fractions were chromatographed for identification. Cerebrosides were measured according to Svennerholm[9] and Radin[10].

Analysis of formalin-fixed and pathological material has several difficulties. With fraction and storage significant modifications of tissue constituents occur. In the presence of abnormal lipids or/and unusual proportions of normal lipid components, the distribution of these tissue components between the several phases may be affected.

In case 1 (Table 1) the amounts of insoluble residue and total lipid were not altered. The decrease in the phosphatide content may be the result of formalin fixation. The percentage of cholesterol esters in the white matter was slightly elevated and the cerebroside content depressed. Both changes can be related to demyelination. Hexosamine was increased in grey and white matter. The ganglioside content of grey matter was slightly increased and that of white matter markedly increased. During fixation in unbuffered solutions and storage the sialic acid moiety may be split from the remainder of the ganglioside molecule, and methods which depend on the measurement of sialic acid for estimation of gangliosides tend to lower results. This consideration is especially applicable to grey matter where changes consequent to fixation and storage occur most intensively. For this reason the hexosamine value in case 1 may be of greater significance (Edgar, G. W. F., personal communication). In this case as well as in case 2 the only sugars obtained following hydrolysis of the ganglioside fractions were galactosamine, galactose and glucose. The relative amounts of these sugars in the gangliosides obtained from pathological material may vary. This observation is now being investigated.

Case 2 (Table 1), which consisted of unfixed frozen tissue obtained several hours *post mortem*, demonstrated an elevation of lipid weight in grey matter. There was a great excess in the amount of lipid nitrogen found in the chloroform phase of the cortical tissue. The lipid nitrogen may be derived in part from gangliosides or their fragments which were distributed in the non-aqueous phase. This observation was supported by the increased amount of hexosamine found in the lipid phase. Also an adaptation of the Warren method[6] applied to the chloroform lipid-rich phase indicated that there were components containing sialic acid in this layer. The ganglioside content of the aqueous phases of grey and white matter extracts, measured both by the Svennerholm[5] and Warren[6] methods, was markedly elevated. As mentioned in case 1, the amino and neutral sugars obtained following the hydrolysis of the ganglioside fraction were quantified, and identified chromatographically as galactosamine, galactose and glucose. The amounts of gangliosides calculated on the basis that they contain about 9 per cent hexosamine and 24 per cent neutral sugars[7] were inconsistent with other data and again suggested either modifications of the gangliosides by the preparative procedures or the disease process, or the variability of methods of hydrolysis, isolation and measurement commonly employed. The remainder of the lipid analysis indicated that the total amounts of phos-

Table 1. Analysis of Brain Tissue of case 1 (age 4 years) and case 2 (age 22 months)

The tissue of case 1 was fixed in formalin, while that of case 2 was frozen immediately *post mortem*. Normal values are to be found in the following references: 11, 12, 13, 14. Grey matter was a sample of frontal cortex, and white the adjacent subcortical region. Phospholipids of grey matter examined by paper chromatography (ref. 4) revealed sphingomyelin in case 2 to be about 11 per cent of the total phospholipids and of a similar amount in case 1. *a*, Calculated value; *b*, method of Svennerholm (ref. 5); *c*, method of Warren (ref. 6). D.W., dry weight of tissue minus proteolipids

Components	Case 1 Grey (per 100 mgm. D.W.)	Case 1 White (per 100 mgm. D.W.)	Case 2 Grey (per 100 mgm. D.W.)	Case 2 White (per 100 mgm. D.W.)
Insoluble residue (mgm.)	63·7	60·4	50·5	58·8
Lipid weight (mgm.)	36·3	39·6	49·5	41·2
Lipid phosphorus (μM)	12·3	15·4	26·2	28·0
Plasmalogen (μM)	—	—	4·3	2·1
Lipid nitrogen (μM)	14·5	16·5	79·5	28·6
Lipid O-acylesters (μM)	23·8	30·8	26·0	46·0
Phosphatides (*a*) (mgm.)	10·2	12·4	21·0	21·8
Cholesterol (mgm.)	8·9	10·6	10·1	10·2
Per cent ester	12·4	17·4	8·0	8·5
Cerebroside (mgm.)	1·82	1·63	0·6	0·4
Hexosamine (mgm.)	0·570	0·370	0·912	0·558
CHCl phase	0·387	0·277	0·785	0·462
Aqueous phase	0·183	0·093	0·127	0·096
Gangliosides (mgm.)				
Aqueous phase (*b*)	2·11	1·34	4·04	2·54
Aqueous phase (*c*)	—	—	3·25	2·15

phatides were within normal limits. There was an increase in lysophosphatides in grey matter noted chromatographically. There was a decrease in plasmalogen and cerebroside content of white matter, suggestive of myelin atrophy.

The main chemical findings support the diagnosis of infantile amaurotic idiocy. The identification of the membranous cytoplasmic granules with the accumulated gangliosides must await isolation of these membranous units and their chemical analysis. Such granules seem to be unique to this condition for they have not been noted in our examination (Terry, R. D., unpublished observations) of other types of lipidoses, nor are they structurally similar to lipofuscin granules. Based on their appearance it is likely that if the membranous units do contain major amounts of gangliosides these glycolipids are associated with proteins to form complex membrane structures.

Whether or not the membranes are derivatives of a normal organelle surface or a coincidental physical formation assumed by excessive or abnormal gangliosides requires consideration. It should be emphasized that there does not seem to be any morphological differences between the granules present in the formalin-fixed tissue and in representative samples from frozen unfixed tissue. This is of particular interest since the sialic acid content of gangliosides decreases with fixation in unbuffered formalin.

There are a number of observations which might indicate considerable order in the molecular constitution of the cytoplasmic granules. There is only limited variation in their structure with two main types being found; their size ranges from 0·5 to 2·0 microns; whenever good resolution was afforded, regular spacing of the membranous elements of their bodies was seen. Some of these issues may be clarified by the study of fractions of homogenized cortical tissue submitted to gradient centrifugation, by which means we have obtained concentrates of these granules.

This work was supported by National Institutes of Health Grants *B*-2255 (*C*1) and *B*-1006 (*C*4). We are indebted to Dr. Bruno W. Volk, director of the Isaac Albert Research Institute of the Jewish Chronic Disease Hospital, for making the material from case 2 available for study.

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THE MOLECULAR DECOMPOSITION OF ALIPHATIC CARBONYL COMPOUNDS

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IT was first shown by Norrish *et al.*[1,2] that the photolysis of the aldehydes and ketones proceeds by two mechanisms, which for methyl propyl ketone are:

Type I $C_3H_7COCH_3 + h\nu = C_3H_7CO + CH_3$ (1)

Type II $C_3H_7COCH_3 + h\nu = C_3H_6 + CH_3COCH_3$ (2)

The first of these is a scission of the bond adjacent to the carbonyl group forming free radicals, and is common to all ketones. The type II reaction is a direct rearrangement into molecular products and is confined to the higher members of the series. This reaction is not limited to the ketones alone but occurs in many other compounds containing a carbonyl group and takes place not only on photolysis but also on thermal decomposition, radiolysis, and electron impact. It is the purpose of this article to assemble the evidence and discuss the nature of the intramolecular split, and to show how the results allow the designation of certain electronically excited states to these molecules.

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The Photochemical Breakdown

The type II reaction was first postulated by Norrish and Appleyard[1] in 1934 in a study of methyl butyl

ketone. Propylene was the major gaseous product and the reaction suggested was :

$$CH_3CH_2CH_2CH_2COCH_3 + h\nu = C_3H_6 + CH_2COCH_3 \quad (3)$$

Later, Bamford and Norrish[2] noted the equivalent reaction with *iso*valeraldehyde and di-*n*-propyl ketone which form propylene and ethylene as their respective olefinic products. As an extension to this work, the photolysis was carried out, both in the vapour phase and in hydrocarbon solution to ascertain the nature of the primary reactions. The method, which utilizes the principle of Frank and Rabinowitsch[3], relies on the free radicals formed in the primary act being confined together in a cage of solvent molecules. At low temperatures, recombination will predominate, lowering the quantum yield, while as the temperature is raised, the yields will be increased due to decomposition and hydrogenation of the free radicals. For a molecular split there is no difference on the change from vapour to solution. Although with di-*n*-propyl ketone, the type I reactions were shown to be exclusively free radical, the type II reaction, characterized by the quantum yield of ethylene, was entirely molecular, being invariant with environment and temperature.

More recently Blacet and Calvert[5] have photolysed butyraldehyde in the presence of iodine and, while the type I products were modified by the radical trap, the yield of ethylene remained unchanged. It was also shown[6] that although *n*-butyraldehyde decomposed intramolecularly, *iso*butyraldehyde formed no type II products. Thus three carbon atoms in a straight chain together with the carbonyl group are required for the reaction to occur.

$$CH_3CH_2CH_2CHO + h\nu = C_2H_4 + CH_3CHO \quad (4)$$

$$(CH_3)_2CHCHO + h\nu = \text{type I products only} \quad (5)$$

Although Wilson and Noyes[7] challenged the view that the type II reaction in the photolysis of methyl butyl ketone was intramolecular as the propylene to acetone ratio in their experiments was not unity, Nicholson[8], repeating the work, found that the ratio remained unity over a wide range of conditions including photolysis in the presence of nitric oxide.

McNesby and Gordon[9], after discovering a variation in product ratio with intensity in the photolysis of partially deuterated methyl propyl ketone, proposed a mechanism based on the interaction of two excited states. This is improbable in view of the solution work, where such a reaction is unlikely, and recently Ausloos and Murad[10], after repeating the experiments, reported no variation.

$$CD_3COCD_2CH_2CH_3 + h\nu = CD_3COCD_2H + C_2H_4 \quad (6)$$

These isotopic experiments indicate that the olefin is certainly formed from the β- and γ-carbon atoms in the molecule.

Experiments with cyclic ketones have thrown some further light on the mechanism : Bamford and Norrish[11] found that while *cyclo*hexanone is photolysed by a type I mechanism alone, l-menthone almost entirely decomposes by a type II reaction.

(7)

The *iso*propyl group is free to rotate and bring the γ-carbon atom close to the carbonyl group as in a free chain. This condition is not fulfilled with *cyclo*hexanone.

The reaction is independent of temperature over a wide range : Masson showed that di-*n*-propyl ketone forms ethylene at a constant rate up to 160° C.[12], while Davies and Noyes showed that the quantum yield of acetone formation from methyl butyl ketone is constant up to 300° C.[13].

The type II split is not limited to the aldehydes and ketones but is also present in the acids and esters. Borrell and Norrish[14] have shown that ethylene is formed intramolecularly in the photolysis of both *n*-butyric acid and its methyl ester :

$$CH_3CH_2CH_2COOR + h\nu = C_2H_4 + CH_3COOR \quad (8)$$

There is no evidence of the reaction with *iso*butyric acid which is thus similar to the isomeric butyraldehydes[6]. Although the carbonyl group is modified by the introduction of a hydroxyl group, the absorption is due to the same transition[15] and the photochemistry should be similar. With a large group in the 'alcohol' position of the ester, another variation is possible : with ethyl acetate, for example, Ausloos[16] found that ethylene forms a large proportion of the gaseous products :

$$CH_3COOC_2H_5 + h\nu = CH_3COOH + C_2H_4 \quad (9)$$

Iodine has no effect on the yield in the vapour phase, and in solution ethylene is formed down to − 70° C.

In addition to the group in the α position having little effect, it is also evident that the reaction is independent of the β group. Ketene is formed in the photolysis of acetic anhydride[17] by the type II reaction :

$$CH_3COOCOCH_3 + h\nu = CH_2CO + CH_3COOH \quad (10)$$

Similarly, methyl ketene is produced from propionic anhydride. Even in very large molecules the reaction takes place, for Guillet and Norrish[18] concluded that the characteristic split occurs in the photolysis of polymethyl vinyl ketone :

$$\begin{array}{l} -CH_2-CH-CH_2-CH- \\ \quad\quad CO \quad\quad\; CO \\ \quad\quad CH_3 \quad\quad\; CH_3 \end{array} + h\nu = \begin{array}{ll} -CH_2-CH_2 & CH_2:C- \\ \quad CO \quad + & \quad CO \\ \quad CH_3 & \quad CH_3 \end{array} \quad (11)$$

Wissburn has confirmed this result[19].

The photochemical studies show that the reaction is intramolecular, independent of temperature, environment and radical traps. It requires at least three carbon atoms in a chain together with the carbonyl group, although the α group may be methylene or oxygen, and the β group may be methylene or another carbonyl group. The cyclic studies indicate that the γ-carbon atom must be free to rotate into the proximity of the carbonyl group.

Thermal Decomposition

In 1876, Oppenheim and Precht pyrolysed ethyl acetate and found the products to be acetic acid and ethylene ; they postulated the reaction[20] :

$$C_2H_5OCOCH_3 = C_2H_4 + CH_3COOH \quad (12)$$

All the work carried out since then has confirmed the mechanism.

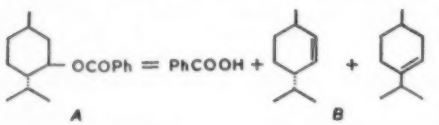
Hurd and Blunk[21], reinvestigating the reaction, pyrolysed several esters in a static system and found that 85 per cent of the decomposition of ethyl and propyl acetates proceeded by an intramolecular split, while *t*-butyl acetate decomposed exclusively by this mechanism. Anderson and Rowley[22] obtained similar results with various formates and showed the reaction to be first order. Blades[23] extended these studies using the toluene flow technique and could detect no evidence of a free-radical mechanism. The results are shown in Table 1.

Table 1

Compound	Activation energy (kcal./mole)	Activation entropy (e.u.)	Ref.
Ethyl formate	44·1	− 10·7	23
Propyl formate	50	− 18·7	22
*Iso*propyl formate	44	− 4·9	23
*Iso*propyl formate	46·3	− 5·35	22
Ethyl acetate	47·75	− 5·4	23
*Iso*propyl acetate	47	− 3·0	23
t-Butyl acetate	39·1	− 4·0	24

The entropies of activation are calculated on the assumption that the transmission coefficient is unity, which is true if no change of electronic state is involved. The activation energies are much smaller than that required for a split into free radicals, and in the absence of any evidence of a chain process, the reaction must be molecular.

Barton[25], in studies of *cis* elimination in terpenes, has pyrolysed (−) menthyl benzoate (*A*), which forms benzoic acid and a mixture of *p*-menth-2-ene (*B*) 36 per cent and *p*-menth-3-ene (*C*) 64 per cent.



(13)

The decomposition is homogeneous and first order; it is considered further in the discussion.

The pyrolysis of acetates has been used for the preparation of olefins and it has been suggested that the reaction forms the least substituted olefin[26,27]; for example, in the pyrolysis of methyl *iso*butyl carbinyl acetate, 4-methyl pent-1-ene is formed exclusively with no 2-olefin.

$$(CH_3)_2CHCH_2CH(OAc)CH_3 = (CH_3)_2CHCH_2CH : CH_2 + CH_3COOH \quad (14)$$

This conclusion, based on a number of studies, has recently been refuted by Royals[28] and Haag and Pines[29]. Reaction 14 in fact only forms 44 per cent of the 1-olefin, the rest being 4-methyl pent-2-ene. Similarly the pyrolysis of 2-butyl acetate yields 1-butene (60 per cent) and 2-butene (40 per cent):

$$CH_3CH_2CH(CH_3)OCOCH_3 \rightarrow CH_3CH_2CH : CH_2 + CH_3CH : CHCH_3 \quad (15)$$

*Iso*propyl chloroformate pyrolyses by two processes[30], one of which forms hydrochloric acid, carbon dioxide and propylene. A type II reaction is obviously occurring:

$$C_3H_7OCOCl = C_3H_6 + ClCOOH = C_3H_6 + HCl + CO_2 \quad (16)$$

but the conclusion should be treated with caution as ethyl chloroformate does not appear to decompose in this way[31].

These various reactions have been extensively studied because the products from pyrolysis are stable at the temperatures of decomposition. With ketones and other carbonyl compounds which may form an olefin and a lower member of the same series, this is not so, for the smaller fragment will decompose too.

As on photolysis (reaction 10), acetic anhydride pyrolyses to form ketene. The molecular nature of this decomposition has been shown by the absence of dibenzyl among the products when Swarc and Murawski studied it, using the toluene carrier gas method[32].

Some sealed-tube experiments with *n*-butyric acid and its methyl ester showed that here too the reaction is present. Ethylene formed a large proportion of the products with butyric acid at 550° C., while it was almost the only non-condensible product from methyl butyrate:

$$C_3H_7COOCH_3 = C_2H_4 + CH_3COOCH_3 \quad (17)$$

The activation energy for this reaction is approximately 34 kilocalories/mole.

The thermal decomposition of these compounds resembles the photochemical reactions. The type II split, which is intramolecular, is the low-temperature form of decomposition, while if the temperature is raised considerably, free-radical products are formed which are consistent with 'type I' reactions.

Electron Impact Studies

The widespread use of the mass spectrometer for analysis has necessitated the tabulation of large amounts of data on a variety of compounds. Sharkey and his collaborators[33] have studied rearrangement peaks in ketones: one significant group is formed by the scission of the β bond to the carbonyl group to form a charged lower ketone. The disadvantage of mass spectral studies is that only one fragment is generally detectable, the other being uncharged, but even so these results are important. Methyl *n*-propyl ketone and higher methyl ketones show a rearrangement peak at mass 58, probably formed by the reaction:

$$CH_3COCH_2(C_nH_{2n+1}) + e = (CH_3COCH_3)^+ + C_nH_{2n} + 2e \quad (18)$$

An analogy to the photochemical results is provided by the absence of a peak at mass 58 with methyl *iso*propyl ketone. Similarly 3-hexanone and larger ethyl ketones form a peak at mass 72 corresponding to the methyl ethyl ketone ion, and *iso*propyl ketones show a re-arrangement peak at mass 86 which corresponds to the methyl *iso*propyl ketone ion. Apparently the molecule splits into an olefin and a charged ketone.

Happ and Stewart, in an earlier investigation of the carboxylic acids[34], noticed a similar effect with *n*-butyric and the isomeric valeric acids which give peaks at mass 60, not formed by the lower acids or *iso*butyric acid. When carbon-13 was substituted into the carboxyl group the peak moved to mass 61, showing that the carboxyl group is present in the ion:

$$C_3H_7{}^{13}COOH + e = C_2H_4 + (CH_3{}^{13}COOH)^+ + 2e \quad (19)$$

Although there have been no other suitable systematic studies, some data are available from the American Petroleum Institute lists[35]. *n*-Butyraldehyde shows

a large peak at mass 44 as does 3-methyl butyraldehyde, which is not present with *iso*butyraldehyde.

$$CH_3CHRCH_2CHO + e = RCH:CH_2 + (CH_2CHO)^+ + 2e \quad (21)$$

Methyl butyrate forms a peak at mass 74 corresponding to the methyl acetate ion, which may be formed in a similar manner.

Esters with a large group in the 'alcohol' position (for example, ethyl acetate) form no significant peaks corresponding to the acid fragment, and any olefin is usually in a region already occupied by type I residues. Some information is provided, however, by chloro- and bromo-ethyl acetates. Chloroethyl acetate forms a peak at mass 62, corresponding to the chloroethylene ion, while bromoethyl acetate shows peaks at masses 106 and 108, consistent with the formation of bromoethylene from the two bromine isotopes:

$$^{79}BrCH_2CH_2OCOCH_3 + e = (^{79}BrCH:CH_2)^+ + CH_3COOH + 2e \quad (22)$$

These esters also do not show peaks corresponding to the acid ion, and it seems that fragmentation may take place in two ways depending on the presence of oxygen in the chain.

$$RCH_2CHR'CH_2COR'' + e = RCH:CHR' + (CH_2COR'')^+ + 2e \quad (23)$$

$$RCH_2CHR'OCOR'' + e = (RCH:CHR')^+ + R''COOH + 2e \quad (24)$$

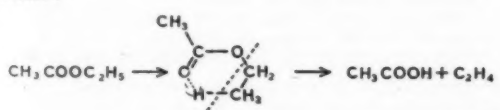
Although it is not possible to detect both of the fragments from electron impact, there seems ample evidence for a type II reaction here.

Radiolysis

In this comparatively new field there has been little interest in the molecules under consideration here. Some aldehydes have been examined but none which might give a type II reaction. However, Ausloos[36] has performed some experiments on ketones and has recorded that ethylene and propylene form a significant proportion of the products when methyl propyl ketone and methyl butyl ketone are radiolysed. Although nothing else has been examined, it is interesting to note that here, too, there is evidence of a type II split.

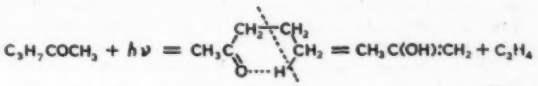
Mechanism of Rearrangement

It is clear that there is a form of decomposition occurring with these large carbonyl compounds, which is virtually independent of environment and conditions, and forms molecular products in a specific manner. For the reaction to be independent of the α and β groups, to break the β bond and to transfer a hydrogen atom from the γ- to the α-carbon atom requires a specific configuration. The most probable mechanism involves the formation of a six-membered ring as an intermediate and the separation of molecular products. This possibility was first put forward by Hurd and Blunk[31] in 1938 for the pyrolysis of esters:



(25)

For this mechanism to occur with a ketone, say, on photolysis, an enol would be formed which must isomerize.

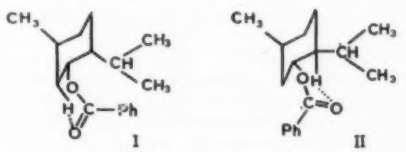


(26)

$$CH_3C(OH):CH_2 = CH_3COCH_3 \quad (27)$$

Srinivasan[37] has shown by his elegant isotopic work that this enol is indeed formed and isomerizes by exchange at the wall of the reaction vessel.

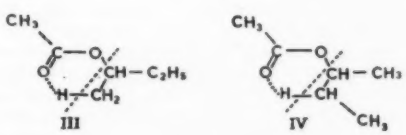
The cyclic intermediate explains the minimum size of the molecules required for this reaction, and provides an explanation for *n*-propyl substituents on the carbonyl group giving type II products while *iso*propyl derivatives do not. The advantage of the cyclic configuration over a flow of protons along the chain, which has also been suggested, is that it is independent of the α and β groups, which may be oxygen or carbonyl. The presence of an additional carbonyl group, as in acetic anhydride, would cause greater strain in the ring, but considering the activation energy required for this approximately thermoneutral reaction, and the transient nature of the intermediate, it should present no difficulty. Barton's work on the pyrolysis of (−) menthyl benzoate[38] is consistent with the ring: there are two positions in which *cis* elimination may occur from the terpene ring:



I II

II is the only conformation available for the formation of menth-3-ene but there is an alternative *trans* linkage to I, which may be preferably formed. Consequently, when elimination occurs, there should be a greater proportion of *p*-menth-3-ene.

The work of Haag and Pines[39] on the pyrolysis of 2-butyl acetate (reaction 15) provides additional evidence, for again there are two possible intermediates:



III IV

In the case of III, which would form 1-butene, there are three hydrogen atoms available for transfer, while with IV there are only two to form 2-butene. Therefore, the yields of 1- and 2-butene should be in the ratio 3 : 2, as in fact is found.

Electronic States of the Larger Carbonyl Compounds

From the previous considerations, it is possible to assign some electronically excited states to these compounds, utilizing the Wigner spin conservation

rule and the results obtained in the photosensitized reactions of several of these compounds. In the mercury photosensitized decomposition of *n*-butyric acid, methyl butyrate, and *n*-butyraldehyde, type I products are formed, but there is no evidence of any intramolecular type II split[14].

There are two established electronic states in the carbonyl compounds, the ground-state and the first excited state. The ground-state is necessarily singlet, as is the upper state formed on absorption of radiation, which raises an electron from a non-bonding orbital localized near the oxygen atom to a less localized antibonding orbital. The transition, designated $n \rightarrow \pi^*$, is forbidden by local symmetry[38]. It is Mulliken's view that the upper state is not repulsive[39], and that photochemical dissociation takes place from other states reached by internal transition. The ground and excited states will be designated here as ^1M and $^1M^*$ respectively.

The type II reaction forms molecular products on photolysis through a mechanism which is independent of temperature or environment, and if spin is conserved the excited repulsive state must be singlet to give rise to singlet products. Although it is possible to postulate a triplet state forming a singlet olefin and a triplet ketone (or vice versa) it is known that triplet ethylene decomposes to form acetylene[40], while it is demonstrated below that triplet carbonyl compounds decompose to type I free-radical products. As it seems unlikely that the singlet 'type II' state is the vibrationally excited ground-state, for this would not be independent of phase and temperature, or the upper $^1M^*$ state, for no type I products would be formed, a separate singlet state ($^1M^{**}$) may be postulated.

The type I free-radical products may be formed from a singlet or a triplet state and the photosensitized results provide a means of distinguishing between the possibilities, for if spin is conserved then the reaction with excited mercury forms a triplet state ($^3M^*$):

$$Hg(^3P_1) + C_3H_7COOH(^1M) = Hg(^1S_0) + C_3H_7COOH(^3M^*) \quad (28)$$

The triplet state gives doublet free-radical products and it seems likely that it does so directly, rather than by internal conversion when type II products would also be formed.

These various conclusions may be conveniently summarized by means of a diagram (Fig. 1), where ethyl acetate is taken as an example. On photochemical excitation, $^1M^*$ state is formed, which gives rise to $^3M^*$ and $^1M^{**}$ states by internal conversion, forming type I and II products. On photosensitization the $^3M^*$ state alone is produced and forms free-radical products directly. Thermal decomposition is brought about by a molecule traversing point *A* from ^1M to $^1M^{**}$ to form type II products, while at higher temperatures the likelihood of crossing is increased and free-radical products are formed. Both electron impact and radiolysis obviously form the upper $^1M^*$ state, which in turn gives rise to type I and II reactions.

By consideration of spin alone, the transition time from the $^1M^*$ to the $^1M^{**}$ state should be faster than that for the $^1M^*$ to the $^3M^*$, and one would expect only type II products to be formed on photolysis. However, the $^1M^{**}$ requires a specific cyclic configuration and the time to form this may well be comparable

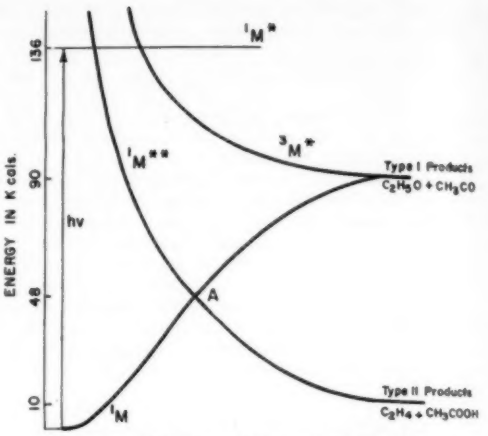


Fig. 1. Potential energy diagram for ethyl acetate

to that for spin reversal. In the photolysis of *n*-butyric acid[14] where the quantum yield is less than unity, it was found that added oxygen increased the yield of type I products while the type II yield decreased slightly. The collision of a free radical, such as oxygen, with the upper excited state might catalyse spin reversal to form a $^3M^*$ state decreasing the number of molecules lost to the ground-state by internal transition and also decreasing the number available for conversion to the $^1M^{**}$ (type II) state.

Although it has been possible to deduce something of the nature of the excited states in these carbonyl compounds, more work is required before their identities are finally settled. The effects of oxygen and other free radicals should provide some useful results, and a correlation of this work and that on the fluorescence of lower ketones may prove fruitful. The thermal decomposition, which is first order, may provide a needed addition to the available examples of unimolecular reactions and it would be useful to study the kinetics at low initial pressures. The change in electronic state in the thermal reaction may be of some theoretical interest.

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SYNTHESIS OF MACROMOLECULES UNDER POSSIBLE PRIMEVAL EARTH CONDITIONS

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OPARIN[1] and Urey[2] have suggested that the primeval atmosphere consisted principally of methane with small amounts of ammonia and water vapour. Miller[3] has shown that when a high-frequency Tesla coil discharge is passed through such an atmosphere, a multitude of organic molecules are produced, including amino-acids. This demonstration of the production of amino-acids has been received with great interest by all those interested in the origin of life, because of their simple chemical relationship to protein material, which seems to hold a key position in present-day life processes. The next step in the sequence of chemical evolution is the production of macromolecules from these simple chemical substances. It is not possible, under ordinary conditions, for the amino-acids to join up spontaneously to form proteins, since the thermodynamic equilibrium is very much in the direction of amino-acids. Fox[4], however, has shown that polypeptides can be made under high temperature (160° C.) and anhydrous conditions. The work described in this communication shows how it would have been possible for macromolecules to have been produced on the primeval Earth.

The apparatus used (Fig. 1) is a 3-l. 'Pyrex' flask with tungsten electrodes sealed through the walls. A mixture similar to the composition which may have existed in the primeval ocean was made up thus: 10 gm. of baker's yeast was ashed at 600° C. and the ash dissolved in 100 c.c. water. Enough concentrated ammonia solution was added to make the solution 1 per cent in ammonia. A stream of hydrogen sulphide was then bubbled through the solution for 10 min. The resulting solution was then placed in the apparatus, evacuated and filled with methane to a pressure of 1 atmosphere. The output of a 40-kV. 50 c./s. transformer was then connected to the two electrodes. The voltage was controlled by a 'Variac' on the transformer primary winding and adjusted to be just below the arcingp oint (approx. 20 kV.). It was difficult to measure the power dissipated in the reaction vessel, but, from the voltage drop across a resistor in the secondary circuit, it was estimated to be of the order of 5 W. At first, after running for 1 hr., a surface-active material was produced, demonstrable by shaking the vessel to produce a foam. After 4 hr., an insoluble transparent film had formed on the liquid – gas interfaces. This material (see Fig. 2) can be produced in more than 10 per cent yield (based on methane). It is insoluble in organic solvents (for example, methyl alcohol, ethyl acetate, acetone, ethyl ether, hexane, benzene and carbon tetrachloride). It is infusible up to 400° C., and at this temperature slowly decomposes. On analysis, this material is found to have the composition C = 75·55, H = 7·33, N = 1·62, S = 0, ash = 3·79 per cent. The infra-red analysis is that of a highly cross-linked polyethylene-type structure with the presence of C=O bands. It has been found that this material will take dyes (for

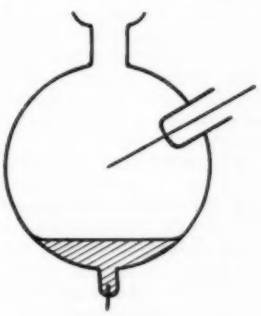

Fig. 1

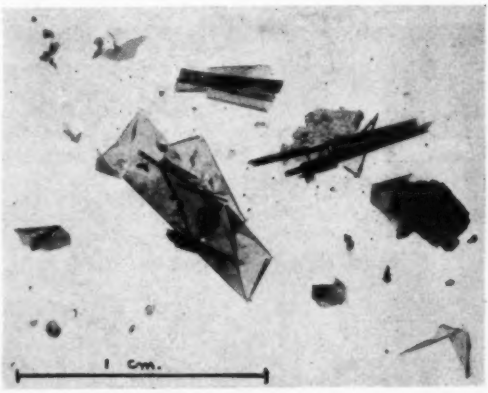

Fig. 2

example, methylene blue and fuchsin), is hydrophilic and more dense than water. (If the ammonia and hydrogen sulphide are omitted from the experiment, a product is obtained which is hydrophobic and cannot be dyed.)

The liquid in the flask was turbid, and when it was examined under the electron microscope, sheet-like molecules were observed (Figs. 3 and 4).

Under the conditions of the experiment, large sheet-like structures are produced. These range in size from large fragments (Fig. 2) through smaller material (Fig. 3) to very small structures (Fig. 4) which are, in fact, macromolecules. The analysis and determination of properties were carried out only on the larger material (Fig. 2), although it might be assumed that this is a reasonable approximation to composition of the material seen under the electron microscope. Thus, high molecular weight polymer is produced from methane, water and ammonia under the influence of an electrical discharge. The combustion results, infra-red spectra and general properties suggest that this polymer is essentially hydrocarbon in nature, and that its surface is covered with polar groups which enable it to be dyed and impart its hydrophilic character.

It seems at first surprising that it is possible to proceed from a simple one-carbon molecule (methane) to what is a product of very high molecular weight. One might expect larger and larger molecules to be built up until the products were no longer volatile, at which stage they would condense out as a liquid. Gas chromatographic analysis of the residual gas in the flask shows that a complicated mixture of $C_1 \rightarrow C_5$ compounds is indeed produced. However, it is difficult to understand how molecules larger than C_{20} could be synthesized without their precursors condensing out. Thus, a liquid product might be expected rather than a solid of very high molecular weight. I suggest that the electrical discharge produces surface-active molecules which form films on the gas – liquid surfaces. These molecules become cross-linked together either directly by the corona discharge itself or by atomic hydrogen produced in the discharge. This mechanism might be expected to produce large sheet-like molecules with one side polar and the other side non-polar. Experiments are in progress to produce similar sheet-like molecules from surface-active materials directly.

If one assumes that the primeval atmosphere of the Earth consisted largely of methane with smaller amounts of ammonia[3], it is reasonable to suggest on the basis of the above experiment that large quantities of hydrocarbons of high molecular weight with surface polar groups could have been synthesized during electrical disturbances on the surface of the primeval ocean and even perhaps on cloud and rain droplets caught in the corona discharge of thunderstorms. This no longer takes place on the Earth because it now has an oxidizing atmosphere, but perhaps it is taking place on the larger planets which still have reducing atmospheres. When one considers the very large number of polar groups of many different kinds all randomly orientated to each other, would it be possible that some of these groupings might be of the right kind and of the right geometrical orientation to endow the macromolecule with 'enzymatic' activity ? (The possibility of completely covering a cloud droplet with this material offers the possibility of having regions within the primeval ocean isolated by a membrane.)

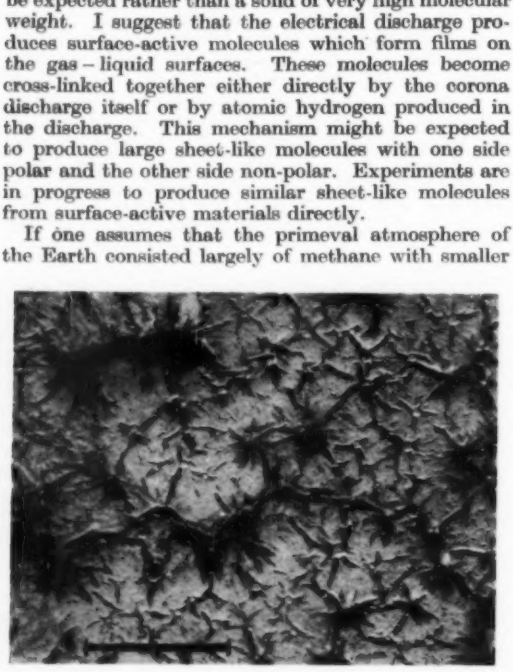

Fig. 3

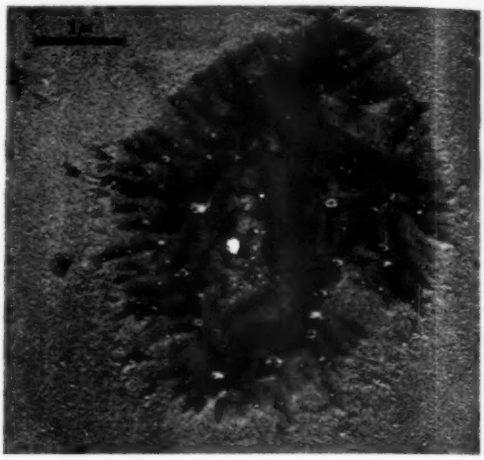

Fig. 4

Thus it is suggested that the early steps in the chemical evolution of life may have been based on catalysts or 'protoenzymes' in which the catalytic groupings were supported on material of hydrocarbon type. This 'hydrocarbon life' would then have evolved until it was sufficiently developed to be able to synthesize its own macromolecules, namely, protein, thus producing the beginning of our present-day 'protein life', where the catalytic groups of the enzymes are supported on protein material. Perhaps the petroleum and shale deposits in the Earth are the debris from the degradation of this material. (If, for example, these proto-enzymes attacked only polar groups and the process of degradation could not progress along the chain past a branch, the residue would be predominantly straight-chain hydrocarbons as are found in petroleum.)

The ease with which this material is produced would lead one to suppose that similar organic material of high molecular weight may be of frequent occurrence in unoxidized cosmic matter and, indeed, organic material of high molecular weight has been found in meteorites[5]. Do the clouds of Venus contain this material ? In this connexion it is interesting to suggest that the fluorescent material[6] found on the surface of the Moon is organic in nature. Also the

gas observed by Kosyrev erupting in Alphonsus[7] (a crater on the Moon) might be explained by the thermal cracking of lunar organic material by radioactive heating.

I wish to thank Dr. A. D. Campbell, of the University of Otago, for the combustion data, the Dominion Laboratory for the gas chromatographic and the infra-red analysis, the staff of the Electron Microscope Section, Dominion Physical Laboratory, for their kind co-operation, and Mr. F. B. Knox for interesting discussions. Much of this work was carried out in the Institute of Nuclear Science, Lower Hutt, New Zealand.

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PERCEPTION OF DISTANCE IN ANIMAL ECHO-LOCATION

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SINCE Griffin and Galambos[1] in 1940 discovered that bats orientate themselves by listening to the echoes from their own sounds, much information has accumulated about echo-location in bats and other animals[2]. Thanks to a number of studies in this field, we now have a fairly extensive knowledge of the acoustical properties of such sounds. There are, however, many questions raised by these studies which have so far received no satisfactory answer.

How, for example, can a bat separate the faint echoes of its own sounds—short, ultrasonic pulses of high intensity—from those emitted at the same time by hundreds or more of other bats? How can they detect and capture an insect when echoes from the ground and countless objects must be returned also? What is the reason for the failure of various attempts to interfere with the echo-locating process, such as trying to jam bats by means of intense noise covering the frequency-range of their pulses[3]?

All efforts to give an answer to these questions are likely to be fruitless while we are uncertain which properties of the echoes the animals utilize in judging distance. Is it the time interval between outgoing pulses and returning echoes or the intensity of the echo or some other property that varies with distance? Whatever the essential property, it is difficult to understand how bats and other echo-locating animals can make any use of the information in the echoes, bearing in mind that the time interval between pulse and echo is of the order of a few milliseconds.

There are, however, some findings from studies in human auditory perception that may help us to get an idea of the mechanism of echo-location. A few years ago Thurlow and Small[4] discovered that two pulse trains of identical repetition rate but slightly separated in time gave rise to a tone the pitch of which corresponded to the magnitude of the time separation. For example, if one train of pulses has a repetition rate of 100 per sec. and a second identical pulse train follows in 1/400th of a sec., the time separation pitch is that of a 400-c.p.s. tone. Decreasing the time separation gradually produces a tone that sweeps upwards (the authors call this phenomenon sweep pitch). Increasing the time separation makes the tone sweep downwards until the difference is half the pulse interval, when the time-difference pitch is the octave of the pulse-repetition frequency, 200 c.p.s. in the above example. A further increase of the time separation makes the tone increase in pitch again. The time-difference pitch thus always corresponds to the shorter time separation. One of the pulse trains may be considerably less intense than the other, particularly if the time separation is small[5]. At a sensation-level of 30 decibels the less-intense pulse train had to be reduced about 17 decibels before the effect disappeared.

There seems to be no reason why bats and porpoises should be different from us in this respect. They will consequently hear a tone the pitch of which corresponds to the time separation between the outgoing pulses and returning echoes, provided the echoes are not too weak. It is tempting to assume that they are also guided in their orientation by these very tones.

If this interpretation is correct, tones in a certain frequency-range have to them acquired a meaning of distance, so that, for example, a rising pitch signifies shrinking distance. If we take into consideration the fact that the echo will return slightly earlier if the animal is moving (although this will affect the result very slightly), a formula expressing the relations involved will be as follows:

$$f = \frac{c + v}{2s}$$

where f is the frequency in c.p.s. that corresponds to the perceived pitch, c and v are the velocity in cm./sec. in the medium (air or water) of sound and animal, respectively, and s is the distance in cm. from the animal's mouth to the object at the moment when the pulse is emitted.

A particularly attractive feature of this mechanism is that the rate of change of pitch is greater close to the object, where the need of accuracy is most acute. As a bat moves from 175 to within 155 cm. of an object, the pitch change will be from about 100–113 c.p.s., whereas an equal change of distance from 40–20 cm. will cause a rise of pitch from about 440–880 c.p.s.

As the lowest audible time-difference tone is unlikely to be much lower than 100 c.p.s., 2–3 metres is probably the greatest distance at which a bat can detect an object by this technique, the corresponding distance for animals living in water being 9–15 metres. This could explain why bats never give any signs in the form of increased pulse rate to show that they

have detected even large objects, such as walls, until they have come within this range. As also thin wires and other objects can be detected at a comparable distance it is possible that some factor other than the intensity of the echoes puts a limit to the distance of detection. Some puzzling results from experiments on a bat's ability to detect wires of different sizes strung across a room may be interpreted in this light. Increasing the size of the wires made the bats show signs of reacting at an increasingly greater distance. As the wire is increased from 1 to 3 mm., however, the distance of detection changes from just less than 2 to not more than about 2·25 metres, which is much less than would be expected[6]. One of the possible explanations for these observations given by the authors is that the bats detect the objects at a greater distance than their data indicate, but do not trouble themselves to increase the pulse rate until they come within a metre or two. For reasons already stated, however, it is possible that they cannot detect objects beyond a certain distance regardless of the strength of the echoes.

We are probably justified in assuming that the time-difference tone can be heard only as a result of a recurrent or a gradually changing pattern, although this aspect of the problem has not been investigated. Every time the animal approaching an object emits a pulse, the time-interval between pulse and echo will be slightly shorter, but the change will be a gradual one. This explains how an echo can be sorted out from among a large number of pulses, such as those from other animals. There is an infinitesimal chance that any two animals' pulses will have exactly the same repetition rate with a constant or gradually changing displacement in time, which are the necessary conditions for a time-difference tone. The pulse rate, moreover, is never absolutely constant, as Griffin's records for the bat *Eptesicus* show, but is slightly irregular even when the mean rate is nearly constant. This is of no consequence for the time-difference tone but makes the animal even less susceptible to interference from other pulses.

There is, however, every reason to believe that echoes from objects at different distances can each give rise to a separate tone, if the relation between pulse and echo is constant. As the pulse repetition rate is never exactly constant, a series of echoes the time lag of which exceeds one pulse-interval can produce no regular pattern and consequently no tone. The same reasoning can be applied to a series of echoes returning in the second half of the pulse interval. The echo will be too far removed from the original pulse, if the findings of Thurlow and Small are applicable under these conditions, and the relation to the next pulse will not be sufficiently constant.

Objects beyond a certain distance depending on the pulse rate can therefore not be detected, at least not by this method. This is probably the reason for the increase in rate as an animal starts to approach an object. As the rate goes up, the zone from which objects return echoes capable of producing a time-difference tone shrinks. At the maximum rate recorded, 200 per sec., a bat would thus not be able to detect anything beyond a distance of about 43 cm. A similar result may be obtained by emitting pulses of gradually reduced intensity or by a combination of both methods.

In this way the porpoise and many types of bats have at their disposal a means of increasing the acuity of their perception analogues to visual accommodation. Another way of excluding irrelevant echoes is to concentrate the emitted sound into a narrow beam. This method is used by some members of the family Rhinolophidae, which thereby compensate for a relatively low maximum repetition rate.

In the calculations above it has been tacitly assumed that the pulse is of negligible duration, and this is not strictly speaking correct. The calculations will scarcely be affected all the same, as Thurlow and Small have shown that the time-difference tone could be heard even when there was an overlap between the pulse trains. It is probably the time difference between the peaks of the sound pressure that determines the pitch. This conclusion is supported by observations recently made by me on pure tones bearing a simple mathematical relationship to one another, such as 1 : 2, 2 : 3, 1 : 3. Varying the phase of one of the tones produces, under certain conditions, a weak time-difference tone the pitch of which corresponds to the time separation between the closest peaks of the sine waves.

Perhaps the most baffling of all problems connected with echo-location has been how bats can discern the faint echoes from thin wires well enough to avoid them even in the presence of thermal noise of much higher intensity. As Thurlow and Small state that they were not able to obtain these tones when thermal noise of various intensities was presented simultaneously with the pulses, this might seem to be a serious objection to my hypothesis.

It is important to note, however, that these experiments were conducted at the relatively low sensation level of 30 decibels, whereas the sound pressure level of the pulses of bats often exceed 100 decibels. I have therefore investigated the effect of thermal noise on pulses of high intensity. The outputs of two pulse generators were led through a narrow band-pass filter and mixed with thermal noise. When the pulses had an intensity of 90 decibels r.m.s. the time-difference tone was clearly audible even when the intensity of one of the pulse generators was considerably reduced and that of the noise was at intermediate level.

Further investigation of the phenomena which have a bearing on the problem of echo-location in relation to rate, composition, and intensity of pulses and echoes is clearly needed. The pulse rate of bats is often only 10 per sec. or even lower, whereas the lowest rate tried on human beings is 25 per sec., when the tone sounded similar to pure tones of short duration[4].

The hypothesis outlined here seems compatible with the acoustical properties of sound produced by many different types of bats, as they are set forth in great detail in a recent paper by Novick[7]. It enables us to understand how these animals can achieve a high degree of precision in their orientation without any corresponding degree of precision in the sound production. The frequency composition, duration, intensity and regularity of the pulses from animals of different types and from one single animal can and do vary within wide limits without serious consequences. Far from being a shortcoming, the irregularity is often, as we have seen, an advantage.

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A SIALOMUCOPEPTIDE LIBERATED BY TRYPSIN FROM THE HUMAN ERYTHROCYTE

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DURING the course of a microanalytical examination of the action of trypsin on the surface of the saline-washed human erythrocyte it was found that a sialomucopeptide was liberated by this enzyme.

Ponder[1] has observed a decrease in the electrophoretic mobility of the erythrocyte on treatment with trypsin. The reduction in mobility corresponds to about a 20 per cent decrease in the net negative surface charge density and is accompanied by an increase in volume of the erythrocyte. Pondman and Mastenbroek[2] suggested from analytical evidence that there is a loss of phospholipid from the erythrocyte on treatment with trypsin. Seaman and Heard[3] were unable to confirm this finding, and suggested that the decrease in mobility is the result of a diminution in the number of α-carboxyl groups effective at the electrophoretic plane of shear.

Trypsin is known to inactivate most mucoproteins which inhibit influenza virus hæmagglutination. Since sialidase inactivates all such inhibitory mucoproteins, presumably by the release of sialic acid[4], trypsin could therefore also release a bound sialic acid. Klenk[5] has demonstrated the presence of a sialic acid (N-acetylneuraminic acid) in the stroma of human erythrocytes.

Standard washed human erythrocytes[6], of phenotypes A Rh+ve, B Rh+ve, ORh+ve and −ve and AB Rh−ve, were examined. 10 c.c. of packed cells per experiment were treated with trypsin (50 μgm./ml.) according to a modification of the method of Morton and Pickles[7]. Appropriately controlled erythrocyte supernatants from each experiment were deproteinized with 20 per cent w/v aqueous trichloroacetic acid, filtered through a No. 50 Whatman paper, reduced to small volume at 50° C. under reduced pressure and the trichloroacetic acid extracted with diethyl ether. The aqueous phase was again reduced in volume and desalted electrolytically.

Finally, these processed supernatants were reduced to dryness and the residues taken up in a few drops of 10 per cent v/v aqueous *iso*propanol. These solutions were examined by descending paper chromatography (Whatman No. 1 paper, butan-1-ol : acetic acid : water (4 : 1 : 5) organic phase). The air-dried chromatograms were dipped in 0·2 per cent w/v ninhydrin in acetone and developed at 90° C.

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Fig. 1 shows schematically the appearance of a ninhydrin-positive compound (purple complex) of R_F 0·65, designated compound 1, from the supernatant of trypsin-treated red cells. This compound is not present in any of the controls. Fig. 2 is a photostat copy of a chromatogram showing components as in strip 1 and strip 5 of Fig. 1.

Compound 1 was eluted with 10 per cent v/v aqueous *iso*propanol from an air-dried untreated controlled chromatogram. The ultra-violet absorption spectrum of eluates of compound 1 shows absorption over the wave-lengths 215–300 mμ with a minor peak at about 270 mμ. Acid treatment of compound 1 produces an increase in the absorption over the range 270–290 mμ (see Fig. 3) and on alkaline treatment there is an increase at 260 mμ (Fig. 4). This spectral behaviour does not suggest trichloroacetic acid contamination and is characteristic of materials containing sialic acid[8].

Microchemical estimations were performed on solutions of compound 1 in 10 per cent v/v aqueous *iso*propanol. The nitrogen content of the eluates was determined colorimetrically by the Nessler method of Johnson[9] and the carbohydrate content was assayed using an anthrone reagent[10]. Sialic acids were determined colorimetrically by the resorcinol–hydrochloric acid method of Svennerholm[11] and the 2-thiobarbituric acid technique of Warren[12]. It was

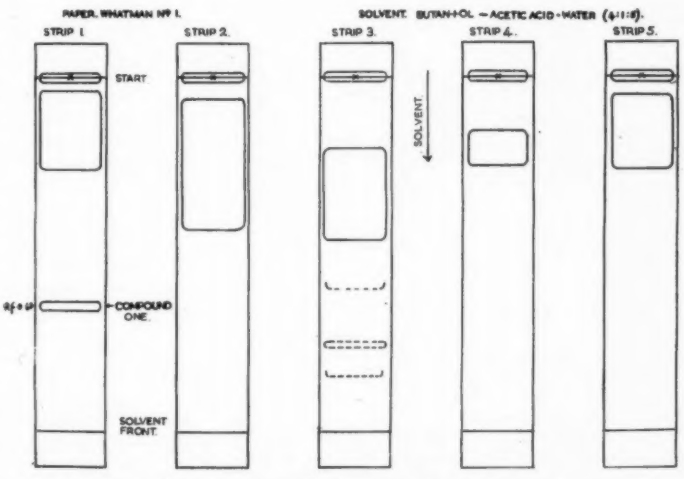

Fig. 1. Map showing regions of ninhydrin-positive material on the chromatograms. Strip 1, supernatant from trypsin-treated human erythrocytes (conc. 50 μgm./ml. total of 2 mgm. trypsin); strip 2, autolysis of trypsin (conc. 50 μgm./ml. total of 2 mgm. trypsin); strip 3, impurities in trypsin (total of 25 mgm. trypsin); strips 4 and 5, supernatants from normal human erythrocytes; (4) incubated in saline (vol. of saline = vol. of saline in strip 1 experiment); (5) supernatant obtained as in strip 4, re-incubated with trypsin (conc. = 50 μgm./ml.). Electrophoretic mobility of untreated erythrocytes = 2·78 ± 0·08μ sec.$^{-1}$ V.$^{-1}$ cm. Electrophoretic mobility of trypsin-treated erythrocytes = 2·30 ± 0·06μ sec.$^{-1}$ V.$^{-1}$ cm.

Fig. 2. Photostat copy of chromatograms developed with ninhydrin, from experiments strip 1 and strip 5. Compound 1 present only in experiment strip 1

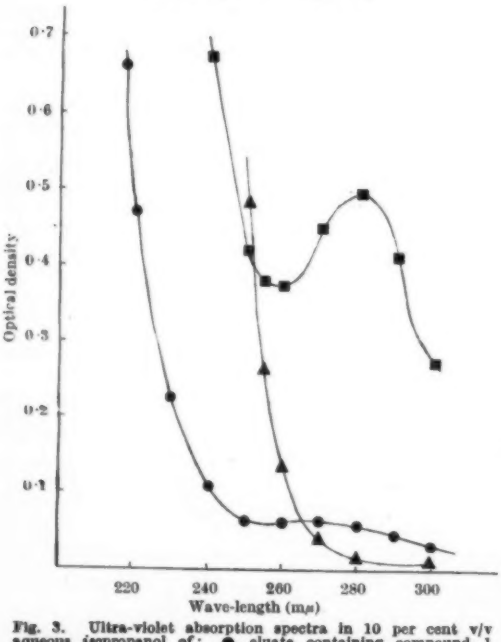

Fig. 3. Ultra-violet absorption spectra in 10 per cent v/v aqueous isopropanol of: ●, eluate containing compound 1 (sialic acid content, 1 μgm./ml.), *p*H 6·1; ■, eluate containing compound 1 (sialic acid content, 1 μgm./ml.) after heating for 10 min. at 90° C., *p*H 2·8; ▲, trichloroacetic acid solution (1,000 μgm./ml.), *p*H 2·0

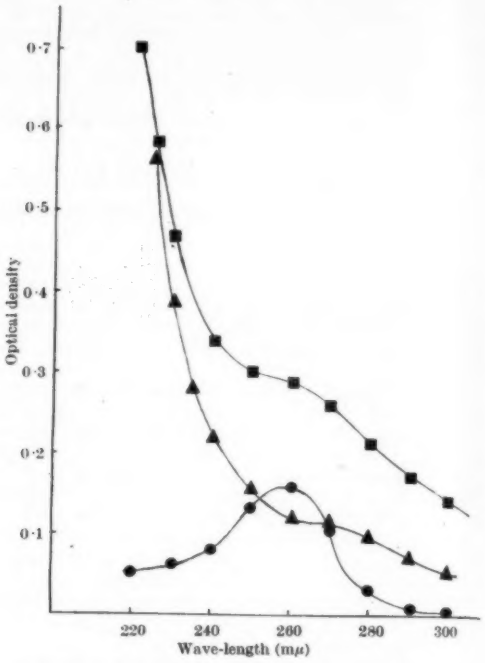

Fig. 4. Ultra-violet absorption spectra in 10 per cent v/v aqueous isopropanol of: ▲, eluate containing compound 1 (sialic acid content, 16 μgm. in 5 ml.), *p*H 5·1; ■, above material reduced to dryness and treated with *N* sodium hydroxide (0·075 ml.) at 105° C. for 17 hr., dissolved in water (5 ml.) adjusted with hydrochloric acid to *p*H 5·8; ●, 2 carboxypyrrole (1 μgm./ml.), *p*H 4·9

found that in compound 1 the ratio of nitrogen to carbohydrate (as glucose) to N-acetylneuraminic acid (after treatment with 0·1 *N* sulphuric acid at 80° C. for 1 hr.) was as 18 : 10 : 1 by weight. The high nitrogen content coupled with the appearance of a purple complex with ninhydrin is indicative of a peptide character for compound 1, which would be expected from the known specificity of trypsin. The release from the periphery of the erythrocyte membrane of this sialomucopeptide, probably structurally analogous to that suggested for ovine submaxillary gland mucoprotein by Gottschalk[13], could account for the decrease in electrophoretic mobility of the erythrocyte observed after treatment with trypsin.

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LETTERS TO THE EDITORS

PHYSICS

Use of an Artificial Satellite to test the Clock 'Paradox' and General Relativity

An interesting and promising test for the effects of gravitation and motion on the relative rates of a satellite clock and an earthbound clock was proposed four years ago by S. F. Singer[1]. For this purpose Singer used the Schwarzschild metric for the Earth's field and considered a circular satellite orbit. The neglect of the ellipticity of the Earth has been justified by B. Hoffmann[2], provided that the mean radius is used. Neglecting also the rotatory motion of the Earth clock Singer found for the red shift of the satellite clock relative to the Earth clock the expression :

$$\Delta = \frac{dt_S - dt_E}{dt_E} = \frac{\gamma M}{2c^2 R}\left(\frac{1 - 2h/R}{1 + h/R}\right) \qquad (1)$$

where R is the radius of the Earth, M its mass, h the height of the satellite above the surface of the Earth, and γ and c have their usual meanings.

However, Singer's calculation is open to criticism, as is also the work of H. Nariai and Y. Ueno[3], who calculate the result for an elliptic orbit following Singer's procedure, since the dt_S, dt_E here are the co-ordinate time-intervals corresponding to unit ticks of the respective clocks. Singer justifies this procedure on the ground that, since t measures proper time for an observer at rest at great distance from the Earth, Δ will therefore measure this observer's view of the relative rates. This is not so since we do not have flat space-time near the Earth where the clocks are. Furthermore, this expression for Δ is not invariant. If we performed a Lorentz transformation at infinity we should find a different value of Δ in terms of the new co-ordinate t'. Finally, we remark that the view of an observer at great distance is not relevant to the practical procedure which Singer suggests for carrying out the test, that is, to make a direct comparison by radio of the cumulative number of oscillations of the two clocks after a suitable number of revolutions of the satellite.

We shall obtain here an invariant form for the expression that Singer desired to measure. As it happens it agrees with Singer's result, but it appears difficult to justify Singer's method of analysis until implied assumptions are clarified. In view of past controversy over the clock paradox, and the need for tests of general relativity, it is thought that a different approach to Singer's test will be of interest.

We formulate in the first instance a slightly different problem from that proposed by Singer. Let a rocket, equipped with a cæsium atomic clock, leave the Earth at a given point and ascend to a suitable height where it goes into free circular orbit about the Earth. Let the rocket complete a suitable number of revolutions and thereafter make a controlled descent to land at the same point of the Earth at which it started. Supposing that the times for ascent and descent are small compared with the time in orbit, we wish to compare the cumulative number of oscillations of the rocket clock with the cumulative total on a similar clock at the rocket base on the Earth.

Following Singer we adopt the Schwarzschild metric for the Earth's field :

$$ds^2 = (1 - 2m/r)dt^2 - \frac{1}{c^2}\left\{\frac{dr^2}{1 - 2m/r} - r^2 d\theta^2 - r^2 \sin^2\theta\, d\varphi^2\right\} \qquad (2)$$

in which $m = \gamma M/c^2$. If we put :

$$v^2 = \left(\frac{dr}{dt}\right)^2 \Big/ (1 - 2m/r) - r^2\left(\frac{d\theta}{dt}\right)^2 - r^2 \sin^2\theta \left(\frac{d\varphi}{dt}\right)^2 \qquad (3)$$

then the element of proper time as registered on the rocket clock will be :

$$ds_{\text{rocket}} = \left(1 - \frac{2m}{r} - \frac{v^2}{c^2}\right)^{\frac{1}{2}} dt \qquad (4)$$

To adequate approximation v is the Newtonian velocity relative to the Earth. Let the orbit be characterized by $\theta = \pi/2$, $d\varphi/dt = \omega$ (constant), $r = a$ (constant). Then the total proper time registered on the rocket clock during the whole journey will be :

$$[s]_{\text{rocket}} = \int_{t_1}^{t_2}\left(1 - \frac{2m}{a} - \frac{\omega^2 a^2}{c^2}\right)^{\frac{1}{2}} dt + \int_{t_0}^{t_1}\left(1 - \frac{2m}{r} - \frac{v^2}{c^2}\right)^{\frac{1}{2}} dt + \int_{t_2}^{t_3}\left(1 - \frac{2m}{r} - \frac{v^2}{c^2}\right)^{\frac{1}{2}} dt \qquad (5)$$

where t_0 is the co-ordinate time of leaving base, t_1 the time of going into orbit, t_2 that of leaving orbit, and t_3 the co-ordinate time of landing at the base. In the last two integrals of (5) r and v will be functions of t.

Similarly, the total proper time registered on the base clock will be :

$$[s]_{\text{base}} = \int_{t_0}^{t_3}\left(1 - \frac{2m}{R} - \frac{V^2}{c^2}\right)^{\frac{1}{2}} dt \qquad (6)$$

where V is the velocity of the base point arising from the Earth's rotation.

But $t_1 - t_0$, $t_3 - t_2$ can be made arbitrarily small compared with $t_2 - t_1$, and so we are able to take :

$$t_2 - t_1 \simeq t_3 - t_0 \qquad (7)$$

and neglect the last two integrals in (5). Furthermore, the geodesic equations of general relativity, as well as the Newtonian theory, yield :

$$\omega^2 a^3 = m\, c^2 \qquad (8)$$

Hence, to sufficient approximation :

$$[s]_{\text{rocket}} \simeq \left(1 - \frac{3m}{2a}\right)\left(t_3 - t_0\right) \qquad (9)$$

and since $V^2 \ll \omega^2 a^2$ for a satellite orbit :

$$[s]_{\text{base}} \simeq \left(1 - \frac{m}{R}\right)\left(t_2 - t_0\right) \qquad (10)$$

Therefore, the invariant fractional excess of the registered time on the Earth clock over that registered on the rocket clock is :

$$\frac{[s]_{\text{base}} - [s]_{\text{rocket}}}{[s]_{\text{rocket}}} \simeq m\left(\frac{3}{2a} - \frac{1}{R}\right) \qquad (11)$$

which, if $a = R + h$, is :

$$\frac{\gamma M}{2c^2 R}\left(\frac{1 - 2h/R}{1 + h/R}\right) \qquad (12)$$

This result has the same interpretation as Singer's. That is, the rocket clock registers the smaller time if $h < \frac{1}{2}R$, and the greater time if $h > \frac{1}{2}R$, or a net red shift and violet shift respectively of order 1 c./s. of the cæsium line.

We could, of course, avoid the necessity of a relatively short period of ascent and descent by requesting the satellite to telemeter its 'readings' for comparison with the base clock from the time of going into orbit to the time of completing a suitable number of circuits, as suggested by Singer. Our result (11) would still apply. But to emphasize that this is a test of the familiar clock paradox, or problem of identical twins, we have chosen to reunite the two clocks at the same space-time event.

In so far as we have deduced the result from the Schwarzschild metric it is also a test of general relativity, that is, of the curvature of space-time that general relativity predicts for the case of a spherical mass.

More strictly, this experiment tests that part of general relativity usually referred to as the principle of equivalence, together with certain features of the Schwarzschild metric which might have been predicted from Newtonian gravitation, in agreement with a view of the Schwarzschild metric recently expressed by H. Bondi and C. W. Kilmister[4].

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Dr. Davidson is quite right in remarking that it is not necessary to introduce an observer at great distance from the Earth in order to measure proper time. But neither is it necessary to bring the two clocks into space-time coincidence at the beginning and at the end of the experiment, as he has done in his derivation. In fact, the experimental method for doing the measurement requires only a comparison of the time intervals necessary to accumulate a large number of ticks on the two clocks, and this comparison could be done by any third observer.

What is interesting is the fact that our derivations do give the same result, as does the derivation superimposing the simple 'red shift' and second-order Doppler shift (from the special theory of relativity). This agreement is not accidental, as Davidson implies. It depends on the fact that the observer at a great distance from the Earth does not carry out any irregular motion ; hence his introduction appears to be correct and entirely equivalent to having, for example, the Earth clock signals themselves determine the co-ordinate time. The reason for this is that the signals travel along null geodesics in a time-independent metric.

I am indebted to my colleague Prof. J. Weber for useful discussion.

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Theoretical Magnetic Moments of Proton and Neutron

Recently it was shown that the equation :

$$E = 38{\cdot}46\ [l(l+1) + s(s+1)]\ \text{MeV}. \qquad (1)$$

provides a correlation of empirical particle masses[1] and of nucleon excitations[2].

The prediction of a resonance energy E_r at 750 MeV. in free protons has now been fully confirmed[3,4]. The maximum for π^+ scattering reported to lie at 1·3 or 1·35 MeV.[3,5] appears to be a doublet as can be seen from Table 1.

Table 1. Calculated and Observed Resonance Energies (MeV.) for Photopions and for Pion Scattering from Hydrogen

Transitions	$^2F_{1/2} \rightarrow$	$^2F_{1/2}$	$^4G_{1/2}$	^2D	$^4G_{1/2}$	^4D	$^4H_{1/2}$	^2F
Pairs created	$2\pi^0$	$2\pi^-$						
E_r calculated	270	279	308	520	577	750	961	980
E_r observed (cm.)	263	279	299	543	574	750	958	983·5
	$\gamma\pi^+$	$\gamma\pi^0$	$\pi^\pm$	$\gamma\pi^+$	$\pi^-,\gamma\pi^0$	$\pi^-,\gamma\pi^0$	π^+	π^+

This table gives the energies for the transitions from the core particle $^2F_{\frac{1}{2}}$ to the indicated higher levels, and the energies needed for the formation of pairs, all calculated according to equation (1). The last line of figures gives the observed resonance energies in photo-production and scattering of pions from free protons.

Equation (1) provides thus a numerical interpretation of all observed resonance energies. The agreement is in several cases within 1 per cent, less than the estimated error.

Equation (1) also contains quantum numbers which are essential for calculating the magnetic moments of the proton and the neutron. In particular, in Table 1, the state $^2F_{\frac{1}{2}}$ plays an important part as the core particle of the proton.

The anomalous magnetic moments of proton and neutron are generally believed to be caused by the contributions of charged (virtual) pions. The magnetic moment of the free pion, however, must be zero. The parity of the pion is odd. Thus it must possess an internal angular momentum, most probably $l = 1$. The correlated magnetic moment is compensated by the anomalous magnetic moment connected with the spin $s = \frac{1}{2}$ of the electric charge. Also the total angular momentum of the pion is zero.

Since the charged pion is required to contribute to the magnetic moment of the nucleon, it cannot be bound in an S-state.

The next simplest case is $l = 1$ for the pion orbital. Then the contribution of the pion to the magnetic moment is one pion magneton :

$$\mu_\pi = (m_p/m_\pi)\ \mu_0 = 6{\cdot}72\ \mu_0 \qquad (2)$$

where μ_0 means one nuclear Bohr magneton and m_P and m_π are the rest masses of proton and pion respectively.

The core particle ${}^4F$ can be assumed to have total angular momentum $I = \frac{1}{2}$ as the ground-state because the system will have minimum energy if the total angular momentum has its minimum value, since then the energy due to the magnetic field connected with the angular momentum will be a minimum.

The ground state of the nucleon is $I = \frac{1}{2}$. The addition of a pion with orbital $l = 1$ to the state ${}^4F_{\frac{1}{2}}$ can lead again to a state with $I = \frac{1}{2}$ as required.

In the case of the neutron the core particle ${}^4F_{\frac{1}{2}}$ can exchange its positive charge with the bound negative pion, since the pion must contain two spins $s = \frac{1}{2}$ to compensate the internal angular momentum to zero. Therefore one spin $s = \frac{1}{2}$ is not occupied by charge.

The probabilities for finding the positive charge at the core or at the pion can be expected to be in the ratio :

$$(2I + 1) : (2l + 3) = 2 : 5 \qquad (3)$$

counting for the statistical weight of the boson, $2 + 1 = 3$ for the bond orbital $l = 1$, another unit for the internal angular momentum $l = 1$ indicated by the odd parity of the pion, and another unit, the sum of the two spins $s = \frac{1}{2}$ which compensate the internal angular momentum of the pion to zero.

The magnetic moment μ_N of the neutron can thus be expected to be :

$$\mu_N = (2/7)\,\mu({}^4F_{\frac{1}{2}}) - (2/7)\,\mu_\pi \qquad (4)$$

The magnetic moment of the core particle $\mu({}^4F_{\frac{1}{2}})$ is not known. The contribution $\mu(F)$ of the F-term ($l = 3$) has to be three core magnetons :

$$\mu(F) = 3(m_P/m_C)\,\mu_0 = 3{\cdot}527\,\mu_0 \qquad (5)$$

The core mass m_C of the state ${}^4F_{\frac{1}{2}}$ is given by equation (1).

Systems with rotational motions belonging to half-integral quantum numbers were investigated by Weyl[6]. In his case, the half-integral quantum numbers are due to the combination of an intrinsic spin $s = \frac{1}{2}$ and an integral quantum number of the type of angular momenta. The magnetic moment due to the spin $s = \frac{1}{2}$ is anomalous, namely, one full unit of a magneton. The quantum number 5/2 should thus lead to three core magnetons and therefore to the same absolute value as given in equation (5). In the state ${}^4F_{\frac{1}{2}}$, however, the two contributions have opposite signs, thus :

$$\mu({}^4F_{\frac{1}{2}}) = 0 \qquad (6)$$

Then, together with (4) and (2) :

$$\mu_N = -\,(2/7)(m_P/m_\pi)\,\mu_0 = -1{\cdot}92_0\,\mu_0 \qquad (7)$$

This value deviates by less than $\frac{1}{2}$ per cent from the empirical value $\mu_N = -1{\cdot}91_3\,\mu_0$. This small difference is probably caused by the relativistic increase of the mass of the pion owing to its kinetic energy.

The result of equation (7) justifies the assumptions made above and leads to the conclusion that the pion is not virtually created but permanently present, and in a well-defined state. The same conclusion was also reached from the mass difference of the nucleon and of the core particle[1].

In the case of the proton, the bound pion has to be neutral. This is the case if the two spins $s = \frac{1}{2}$ within the pion are occupied by opposite charges. Then there is no spin $s = \frac{1}{2}$ free of charge and the exchange of a single charge between core and pion which occurs within the neutron is no longer possible within the proton.

According to equation (1), however, there is the possibility of resonance between the isobaric states ${}^4F_{\frac{1}{2}}$ and ${}^2G_{7/2}$. The probabilities for finding the core particle in these states are in the ratio 2 : 8, due to the respective values of $2I + 1$.

Then the resulting magnetic moment of the core should be :

$$\mu_C = (0{\cdot}2)\,\mu({}^4F_{\frac{1}{2}}) + (0{\cdot}8)\,\mu({}^2G_{7/2}) \qquad (8)$$

The magnetic moment of the state ${}^2G_{7,2}$ must be 4–1 = 3 core magnetons, incidentally the same value as given in (5). This value together with (6) and (8) leads to :

$$\mu_C = (0{\cdot}8)3(m_P/m_C)\,\mu_0 = 2{\cdot}82\,\mu_0 \qquad (9)$$

This value deviates only about 1 per cent from the empirical value of the magnetic moment of the proton $\mu_P = 2{\cdot}79\,\mu_0$. The difference is presumably due to diamagnetism of the neutral pion contained in the proton.

In the resonance process between the isobaric states of the core, the total angular momentum would not be conserved. This condition can be fulfilled in the case of the proton if the angular momentum of the bound neutral pion changes from $l = 1$ with core ${}^4F_{\frac{1}{2}}$ to $l = -3$ with core ${}^2G_{7/2}$.

The neutral pion can be bound to the core by the exchange of the positive charge of the core and of the positive charge which neutralizes the negative charge in the neutral pion. This process would not change the magnetic moment of the system.

The resonance process within the proton between the two isobaric core states ${}^4F_{\frac{1}{2}}$ and ${}^2G_{7/2}$ introduces also an unsharpness of the two states and widens the energy range in which resonance can occur.

If the bound pion were not neutral, additional energy would be required to build up the magnetic field connected with the orbital $l = 3$. This would destroy the condition for resonance which exists for the system of core and bound neutral pion. In fact, the ensuing magnetic moment would also destroy the agreement with the empirical values.

Thus the resonance process between the isobaric states ${}^4F_{\frac{1}{2}}$ and ${}^2G_{7,2}$ appears to be possible only in the case of the proton with its neutral pion, but not for the neutron as a compound of a positive core and a negative pion. In this way one can understand the exceptional stability of the proton.

Like the proton, the Ξ-particle appears to contain a neutral pion. The rest energy of the charged Ξ-particle is 1,319 MeV., and this is quite near the sum of a ${}^3H_{3/2}$ particle and of a neutral pion, namely, 1,182 + 135 = 1,317 MeV.

The agreement between calculated and empirical values of the magnetic moments of proton and neutron indicates that the half-integral quantum numbers s in equation (1) refer really to Weyl's relativistic system of spherical harmonics with spin.

The quantum numbers of equation (1) must belong to internal degrees of freedom of extended particles, and this equation appears now to be relevant to the calculation of the masses of the 'elementary'

heavy fermions, of the internal excitation energies of the free proton and of the magnetic moments of proton and neutron.

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Generation of Water Waves by the Wind

The spectral energy density φ of small deep-water waves increases with wind speed and fetch, for a given frequency-band, only up to a certain value. For larger wind speed or fetch the energy density appears to become saturated, as was noticed by Burling[1] and by Phillips[2]. Having recently completed a detailed analysis of two sets[1,3] of data on φ, I can now give quantitative evidence for this apparent saturation. (I am indebted to Dr. Burling and to the Imperial College of Science and Technology, London, for permission to use the original data published in his thesis.)

For the purposes of the analysis I assumed φ to be of the form :

$$\begin{aligned} \varphi &= b_1 V^{r_1} F^{s_1} f^{t_1} \quad f \leqslant f_0 \\ &= b_2 V^{r_2} F^{s_2} f^{t_2} \quad f > f_0 \end{aligned} \tag{1}$$

where V, F, and f are the independent variables in the experiments, that is, the average wind speed, the average fetch, and the wave-frequency. The eight parameters, b_1, b_2, r_1, r_2, s_1, s_2, t_1, and t_2, are at our disposal in making the best fit to the experimental data. On the basis of earlier analyses we can expect that r_1, s_1, t_1 and $-t_2$ will be positive, the opposite signs of t_1 and t_2 implying that the largest value of φ, for given V and F, is reached at $f = f_0$. The value of f_0 is given by the equation :

$$b_1 V^{r_1} F^{s_1} f_0^{t_1} = b_2 V^{r_2} F^{s_2} f_0^{t_2} \tag{2}$$

For a frequency $f < f_0$, the spectrum is unsaturated. For a frequency $f > f_0$, the spectrum is saturated with respect to increases of wind speed or fetch if the absolute values of r_2 and s_2 are small compared to one. (Phillips refers to the saturated part of a spectrum as the "equilibrium range".) More complete descriptions of wave generation than these equations afford would require the specification, for example, of the velocity profile above the water and the directional spectra of the wind and of the waves.

Burling's data consist of 463 measured values of φ for various combinations of frequency, average wind speed, and average fetch in the ranges :

$$0{\cdot}4 \leqslant f \leqslant 1{\cdot}8 \text{ c.p.s., } 5{\cdot}0 \leqslant V \leqslant 8{\cdot}8 \text{ m./sec.,}$$
$$\text{and } 400 \leqslant F \leqslant 1{,}350 \text{ m.}$$

All the wave systems that he studied were thus in the gravity wave regime. My data consist of 273 measurements of the wave energy, observed through octave-wide filters centred at 0·75, 1·5, 3, 6 and 12 c.p.s., for various combinations of average wind speed and average fetch in the ranges :

$$0{\cdot}15 \leqslant V \leqslant 10{\cdot}2 \text{ m./sec. and } 5 \leqslant F \leqslant 625 \text{ m.}$$

Most of the waves that I measured also were in the gravity wave regime. Integration of the function φ in equation (1) over the power transfer function of the filter yields energy values which can be compared with my experimentally determined values. For each of the two sets of data a least-squares fit was made to find the best values of the eight parameters in equation (1). Afterwards, 10 sub-sets of data were chosen at random from each set of data, and least-squares fits, starting with randomized values of each parameter, were made for each of the 20 sub-sets. I shall discuss here the results of my analysis only for the parameters r_2, s_2, t_2 and b_2.

In Table 1 are listed, for each set of data, the best values of these four parameters and the probable errors, parameters and errors both being derived from the randomly chosen sub-sets.

Table 1

	r_2	s_2	t_2	$\log_{10} b_2$*
Burling	$0 \pm 0{\cdot}02$	$0 \pm 0{\cdot}01$	$-5{\cdot}69 \pm 0{\cdot}04$	$-3{\cdot}10 \pm 0{\cdot}02$
Present author	$0{\cdot}41 \pm 0{\cdot}14$	$-0{\cdot}14 \pm 0{\cdot}05$	$-4{\cdot}66 \pm 0{\cdot}12$	$-2{\cdot}78 \pm 0{\cdot}22$

* m.sec. units.

For the limited range of frequency in Burling's data r_2 and s_2 may be taken equal to zero with a high degree of certainty. For the larger frequency-range of my data, r_2 and s_2 may also be taken to be about equal to zero. In fact, if in the least-squares analysis of my data $r_2 = s_2 = 0$, the best values of the other two parameters are essentially unchanged from the values given in Table 1. It may be concluded then that the saturation effect noted by Burling and by Phillips does indeed exist and that it extends over a frequency-range that is more than a decade wide.

The two values of $\log_{10} b_2$ given in Table 1 differ by but little more than the sum of the probable errors. The exponents t_2 from the two sets of data do not agree within their combined probable errors. The value -5 or $-2{\cdot}33$ for this exponent is to be expected for pure gravity waves or pure capillary waves, respectively, if the wave growth is affected only by the acceleration of gravity or by the capillary constant. That t_2 for my experiments is smaller in absolute value than for Burling's experiments may reflect the fact that some of the waves I measured are in the capillary–gravity wave regime. It should also be pointed out that the air boundary layers, for the same wind speed and fetch, were probably rather different in Burling's experiments and in mine.

Small gravity waves may well form a naturally occurring dynamical model of the larger wind waves on the ocean. If a dynamical similarity does exist, then it would be expected that ocean waves will show a saturation effect similar to that of the smaller waves and that wind waves of the two scales will be alike in many other respects. Model work on small waves on lakes and reservoirs would then provide, with but a small effort, data on wind wave generation that are significant for the waves both on lakes and on the sea. The critical question is : How complete is the supposed dynamical similarity between the generation by the wind of large and small gravity waves ?

The CSL measurements were made by E. A. Huber and C. G. Whittenbury. Calculations were made on *Illiac*, the digital computer of the University of

Illinois. G. Berg and C. W. Mendel wrote most of the *Illiac* programmes used in the data reduction. This work was supported by a Tri-Services Contract of the Department of Defense.

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Standard Unit of Pressure in Vacuum Physics

DR. N. A. FLORESCU[1] proposes to use in vacuum physics a unit of pressure = 10^3 dynes cm.$^{-2}$, which he suggests should be called a 'vac'. A unit of this magnitude, however, has already been designated and used under the name 'millibar', and is equal to 100 newtons m.$^{-2}$. It therefore seems to me useless to invent a new name, particularly at a time when attempts are being made to limit the introduction of special names for units derived from systems in current use.

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MANY readers of Dr. Florescu's communication in *Nature* of October 22, p. 303, on the standard unit of pressure in vacuum physics will see in it a powerful plea for the extended use of the absolute unit of pressure, the bar equal to 10^6 dynes/cm.^{2}. They will of course recognize that the proposed 'vac' is none other than the existing millibar (see, for example, British Standard 2520 (1954). Barometer Conventions and Tables). Now that the internationally adopted prefixes to abbreviations for the names of the metric units are coming increasingly into use (see for example B.S. 1991, Part 1 (1954), Symbols, Signs and Abbreviations, p. 32) there should be no difficulty in applying them to the bar and thus realizing the objective which Dr. Florescu has in mind. There is no need to introduce a new unit. For example, we have:

1 vac	=	10^{-3} bar	= 1 millibar (mb)
10^{-3} vac	=	10^{-6} bar	= 1 microbar (μb)
10^{-6} vac	=	10^{-9} bar	= 1 nanobar (nb or mμb)
10^{-9} vac	=	10^{-12} bar	= 1 picobar (pb or $\mu\mu$b)

(In each instance the abbreviation 'b' for bar can, according to a 1948 decision of the General Conference of Weights and Measures, be replaced by the complete word 'bar'.)

Regarding Dr. Florescu's plea that the millibar (or 'vac') should be recognized as granting a special significance to the value 980·7455 cm./sec.^{2} for gravity, this should be approached with considerable reserve, bearing in mind the confusion which existed for many years between various other values associated with the term standard gravity (see B.S. 2520 (1954), p. 6). This confusion was resolved in 1950 by the International Committee of Weights and Measures when the value 980·665 cm./sec.^{2} was re-affirmed as standard. This value is now accepted as standard for all purposes, and it is to be hoped that no action tending towards further confusion will now be taken.

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GEOPHYSICS

Effects of Diffusion of Electrons near the Magnetic Equator

IN a recent interesting communication, Dr. E. R. Schmerling[1] has discussed the possible effect of vertical diffusion in the ionosphere in the presence of the geomagnetic field. He claims that the effect of diffusion is to increase the electron density below the electron peak, so that near the magnetic equator the electron density N at a given height h should be less than in slightly higher latitudes, since the magnetic field at the equator is horizontal and precludes vertical diffusion. Dr. Schmerling, however, assumes in this derivation that the rate of ion production is independent of latitude and therefore of the magnetic dip.

If we assume that the ionization is produced according to the Chapman law, this is certainly not the case, the rate of ionization increasing as the magnetic equator is approached. The two effects therefore tend to cancel each other out, and according to our calculation it seems that the increase in ionization at lower geomagnetic latitudes exceeds any decrease due to the effects of diffusion described by Dr. Schmerling. This is illustrated in Fig. 1, which shows the variation of electron density with geomagnetic latitude about an hour after midday at heights of ½, 1 and 1½ scale heights above the level of maximum ion production. The graph of maximum electron density (N_m) follows very closely the highest curve in Fig. 1, and we must conclude that the $F2$ model under discussion, based on a hypothesis of

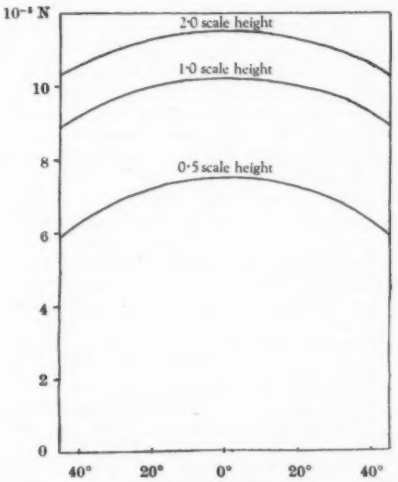

Fig. 1

vertical diffusion, does not account for the Appleton anomaly. It will be seen from this figure that the variation of electron density at midday is rather insensitive to changes of geomagnetic latitude. It has been suggested by various writers, however, that horizontal diffusion may affect the vertical distribution of ionization, and near the magnetic equator the tendency would be for ionization to diffuse away north and south from the equator and pile up on opposite sides of it. We are at present investigating the magnitude of this effect.

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Evidence of Quasi-Perpendicular Propagation of Hydromagnetic Waves caused by Nuclear Explosions over Johnston Island

In previous reports[1,2] one of us (H. M.) has suggested that the initial phase of artificial magnetic storms due to high-altitude nuclear explosions over Johnston Island (16·5° N.; 169·5° W.) may be interpreted by hydromagnetic waves propagated through the high atmosphere from the explosion point. Such a suggestion has also been made by many other workers. The purpose of this communication is to exhibit evidence supporting such a suggestion. (Quite recently, Berthold *et al.*[3] have also found similar effects due to *Argus*.)

Fig. 1 shows replotted recordings of the induction magnetograph around 10h. 50m. G.M.T. on August 1, and around 10h. 30m. G.M.T. on August 12, 1958, at Shimosato (33·6° N.; 135·9° E.) and Onagawa (38·4° N.; 141·5° E.) in Japan. As has been estimated by Maeda[3], the explosion time (and altitude) is 10h. 50m. (150 km.) on August 1, and 10h. 30m. (70 km.) on August 12, respectively. On examining carefully the magnetic traces, one finds peculiar changes around the explosion time on each day. The changes seem to consist of two parts, the first and the second arrivals, and each of them starts at the time indicated by arrows, and comes to an end about 30 sec. later. An almost complete similarity between the changes on both days at each station seems to provide the evidence that these changes are the direct effect of the Johnston Island explosions. Numerical detail of the changes read from magnetograms is summarized in Table 1.

It seems likely from these results that the changes found at Japanese stations are due to hydromagnetic waves propagated in the high atmosphere across the lines of geomagnetic force from the explosion point. If so, the propagation velocity is estimated at about 540 km./sec. for the first arrival, and about 300 km./sec. for the second arrival, on the average. Moreover, if we assume that the initial change at Honolulu is also caused by hydromagnetic waves, the average damping distance in which the wave is attenuated by a factor e^{-1} is estimated at about 1,650 km.

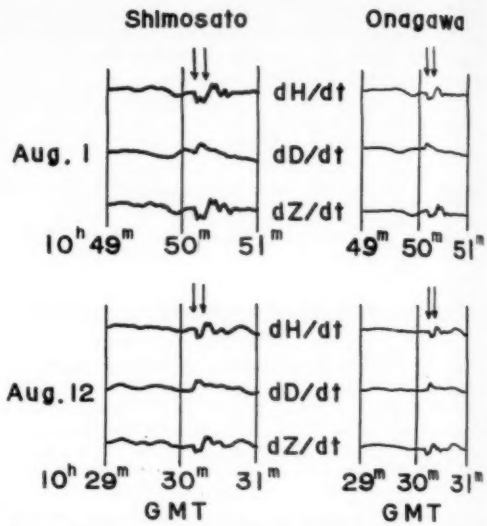

Fig. 1. Replotted recordings at Shimosato and Onagawa, Japan, showing geomagnetic effects due to Johnston Island nuclear explosions on August 1 and 12, 1958

As seen in Fig. 2, the propagation path is across the lines of geomagnetic force at about 90° (that is, quasi-perpendicular propagation), so that the waves seem to be a modified Alfvén mode. Theoretical treatment of the propagation of hydromagnetic waves in a partially ionized plasma has been carried out by Akasofu[4], Dungey[5] and Piddington[6,7]. According to Piddington's formulæ, the propagation velocity and the damping distance depend closely on altitude in the ionospheric region. The damping distance of about 1,650 km. estimated here corresponds to an altitude of about 300 km. On the other hand, the propagation velocity at this altitude is about 10 km./sec. This value is much smaller than that deduced here. Such a disagreement results from a very simple assumption that the hydromagnetic waves are propagated along a path of constant height in the ionosphere. The actual conditions of propagation, however, seem to be much more complicated.

Thus, although it seems, at present, to be difficult to find any precise interpretation of the phenomena, the following preliminary picture may be drawn. Simultaneously with high-altitude nuclear explosions, very strong shocks are caused and propagated with high velocity. These shocks are attenuated after travelling some distances, and degenerate into hydromagnetic waves (of the modified Alfvén mode

Table 1. Numerical Detail of Geomagnetic Changes at Shimosato

	First arrival				Second arrival				Last time of arrival (sec.)
	Time of arrival (sec.)	dH/dt	Amplitude dD/dt (γ/sec.)	dZ/dt	Time of arrival (sec.)	dH/dt	Amplitude dD/dt (γ/sec.)	dZ/dt	
August 1	9	0·058	0·045	0·080	18	0·090	0	0·135	41
August 12	11	0·051	0·042	0·060	18	0·066	0	0·105	40
Mean	10	0·055	0·044	0·070	18	0·078	0	0·120	41

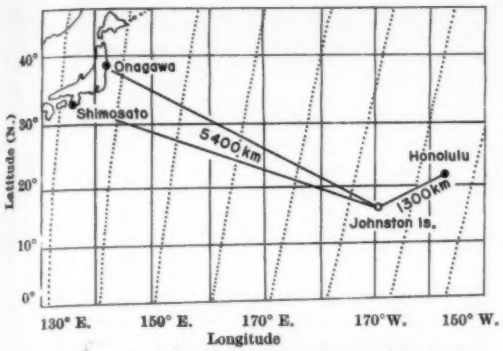

Fig. 2. Distance and direction from Johnston Island to observed stations, where dotted lines indicate the geomagnetic meridian

in the present case). The hydromagnetic waves will be propagated through the upper ionospheric region in the following manner: a highly ionized plasma produced by explosions pushes the geomagnetic field away, as it expands, so that a magnetic barrier may be formed in a height where the magnetic pressure of the compressed geomagnetic field equals the kinetic pressure of the plasma. Because of such a barrier, the waves may tend to be propagated horizontally; and its height seems to be lower (probably around 900 km.) than that suggested by Bomke *et al.*[8], because both the height and the latitude of Johnston Island explosions are lower than those of *Argus*. The first and the second arrivals found here would not be due to the difference of propagation mode, but due to the difference of propagation path. If several induction-type magnetographs of high sensitivity had been used, the effects of the explosions would also be detected at more distant stations than Japanese ones.

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RADIATION CHEMISTRY

Radiation-induced Carboxylation of Organic Compounds: Formation and Reactions of the Carboxyl Radical Ion

WE have recently reported[1] some results on the reduction of carbon dioxide and bicarbonate in aqueous solution by cobalt-60 γ-rays and X-rays, leading to the formation of formic acid, aldehydes and small quantities of oxalic acid.

It has been found also that under these conditions the yields of molecular hydrogen were low when carbon dioxide or bicarbonate was present in the solution. From work on these reactions under different *p*H conditions, one is led to the conclusion that the negatively charged polarons $(H_2O)^-$, formed by the action of the radiation on water[2], which can react, for example, with protons according to: $(H_2O)^- + H^+ \rightarrow H + H_2O$, can, in the presence of carbon dioxide or bicarbonate, react as follows[2]:

$$(H_2O)^- + CO_2 \rightarrow CO_2^- + H_2O \quad (1)$$

$$(H_2O)^- + HCO_3^- \rightarrow CO_2^- + OH^- + H_2O \quad (2)$$

The existence of the CO_2^- radical ion in aqueous systems has recently been postulated also from polarographic evidence[3].

Some of the reduction products observed in the radiolysis of solutions of carbon dioxide or bicarbonate are the result of further reactions of the CO_2^- primarily formed (or the corresponding COOH radical with which it will be in equilibrium according to: $CO_2^- + H^+ \rightleftarrows CO_2H$); for example, dimerization of these radicals can lead to oxalic acid.

Furthermore, direct proof of the presence of CO_2^- has been obtained from experiments in which oxygen-free aqueous solutions containing suitable organic solutes (for example, alcohols, acids, aliphatic hydrocarbons, etc.) are irradiated in the presence of carbon dioxide or bicarbonate. Under these conditions, it has been clearly demonstrated that the reduced carbon dioxide can be built into the organic molecules with the formation of the corresponding carboxylic acids.

For example, irradiation of aqueous solutions of ethanol (10^{-3} *M*) in the presence of carbon dioxide (0·5 atm.) or sodium bicarbonate (10^{-3} *M*) with cobalt-60 γ-rays (dose-rate $1{\cdot}8 \times 10^{17}$ eV. ml.$^{-1}$ min.$^{-1}$) gave lactic acid; the yields obtained were dependent upon *p*H, varying between $G \sim 1$ (molecules/100 eV.) at the lower *p*H to $G \sim 2$ at the higher *p*H. The lactic acid was identified by paper chromatography. Similar experiments were also carried out with carbon dioxide or bicarbonate labelled with carbon-14; in the latter case identification and analysis were carried out by isotope dilution technique.

Under similar conditions, irradiation of aqueous methanol gave glycollic acid, and irradiation of dilute acetic acid solutions gave malonic acid. When a solution of a 1 : 1 mixture of methane and carbon dioxide (total pressure 1 atm.) was irradiated with γ-rays, acetic acid was found to be one of the radiation products. Irradiation of 10^{-2} *M* formic acid in the presence of carbon dioxide labelled with carbon-14 (2×10^{-2} *M*) at *p*H 3·5 gave oxalic acid with a yield of $G \sim 1{\cdot}2$, calculated as ^{14}COOH.COOH (unpublished results of N. Getoff and M. Simic).

All these experiments were carried out in deoxygenated solutions; this is of importance, because otherwise the negative polarons may be scavenged to a greater or lesser extent by molecular oxygen according to: $(H_2O)^- + O_2 \rightarrow O_2^- + H_2O$, as shown previously[2].

In general, the carboxylation process depends on the formation of a free radical from the organic solute by the action of the OH or $(H_2O)^+$ formed by the ionizing radiation acting on the water, and association of the organic free radical with the CO_2^- radical ion formed according to reactions (1) or (2).

In the formation of lactic acid from ethanol, one has the following reactions:

$$CH_3CH_2OH + OH \rightarrow CH_3CHOH + H_2O \quad (3)$$

$$CH_3CHOH + CO_2^- \rightarrow CH_3CHOH\,CO_2^- \quad (4)$$

Similarly, glycollic acid is formed via the radical CH_2OH produced by dehydrogenation of methanol.

The production of acetic acid from methane and carbon dioxide would involve a CH_3 radical as follows[4]:

$$CH_4 + OH \rightarrow \dot{C}H_3 + H_2O \quad (5)$$

$$CH_3 + CO_2^- \rightarrow CH_3CO_2^- \quad (6)$$

Formation of malonic acid from acetic acid is according to the following reactions:

$$CH_3CO_2H + OH \rightarrow CH_2CO_2H \quad (7)$$

$$CH_2CO_2H + CO_2^- \rightarrow {}^-O_2C\,CH_2\,CO_2H \quad (8)$$

It has been shown also that irradiation of more complex polymer molecules, such as histones and nucleoproteins, in aqueous systems, in the presence of carbon dioxide, leads to the introduction of carboxyl groups into the molecules; this has been demonstrated using carbon dioxide or bicarbonate labelled with carbon-14 (Appleby, Emmerson, Scholes and Weiss, unpublished results).

Carboxylations with CO_2 in the gaseous state or in mixtures with solid carbon dioxide under the action of 2-MeV. electrons have been reported recently; in these cases the carboxyl compounds appear to be relatively minor reaction products as they are only formed with yields of $G = 0{\cdot}01 - 0{\cdot}1$ (ref. 5).

It is clear that in this way it is possible to produce labelled carboxylic compounds and, in particular, to produce some carboxylic acids labelled with carbon-14 which may be difficult to obtain in any other way.

Another application of this method of radiation-induced carboxylation would be its use in the identification and characterization of free radicals produced by radiation, as in this way the radicals could be converted into carboxylic acids which may then be identified as such, for example, by an isotope dilution technique, if carbon dioxide or bicarbonate labelled with carbon-14 is used for the carboxylation process.

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CHEMISTRY

Heats of Chemisorption of Simple Diatomic Molecules on Metals

There have been suggestions recently that the heats of formation of compounds are related to the catalytic activity of metals and heats of chemisorption[1-3]. Fahrenfort, van Reijen and Sachtler have shown that for the decomposition of formic acid on metals there is a definite correlation between the activity of the metal and the heat of formation of the metal formate. A relationship between heats of oxygen chemisorption and heats of oxide formation is suggested by the recent results of Brennan, Hayward and Trapnell.

Table 1. Heats of Formation are taken from "Selected Values of Chemical Thermodynamic Properties" by Rossini

Compound	$-\Delta H°_f$ (298·16° K.) kcal. mole^{-1}	$-\Delta H$ (calorimetric) kcal. mole^{-1}	Ref.
NiH	2·7	35	4
NiO	58·4	110	3
FeO	63·7	130	3
CoO	57·2	110	3, 5
MnO	92·0	150	3
PdO	20·4	67	3
RhO	21·7	76	3
TaN	58·2	130	4
WO_3	136·3	190	3
TiO_2	218	235	3
CrO_2	138·4	170	3
AlO_2^-	218·6	210	3
NiS	17·5	—	

If, as a first approximation, the assumption is made that during chemisorption of diatomic molecules a two-dimensional surface compound is formed of simple stoichiometry, it would be anticipated that a correlation should exist between the heat of formation of that compound and the heat of chemisorption. Table 1 gives values for the heats of chemisorption (ΔH) of simple diatomic gases on metals determined calorimetrically and the corresponding heat of formation ($\Delta H°_f$) of the stoichiometrically simplest compound. For example, in the oxidation of cobalt the heat of chemisorption is compared with the heat of formation of CoO and not Co_3O_4. An interesting example is the oxidation of aluminium where the heat of formation of AlO_2^- is used and not that of Al_2O_3. There does not appear to be any reason *per se* why the chemisorbed oxide layer on aluminium should not, in fact, have the composition AlO_2^-. In Fig. 1 are plotted the heats of chemisorption (experimental accuracy $\pm$ 5 kcal. mole^{-1}) and the corresponding heats of formation of the stoichiometrically simplest compound.

Since values for the heats of chemisorption of gases are somewhat limited the correlation shown in Fig. 1 allows estimates to be made of such heats if the

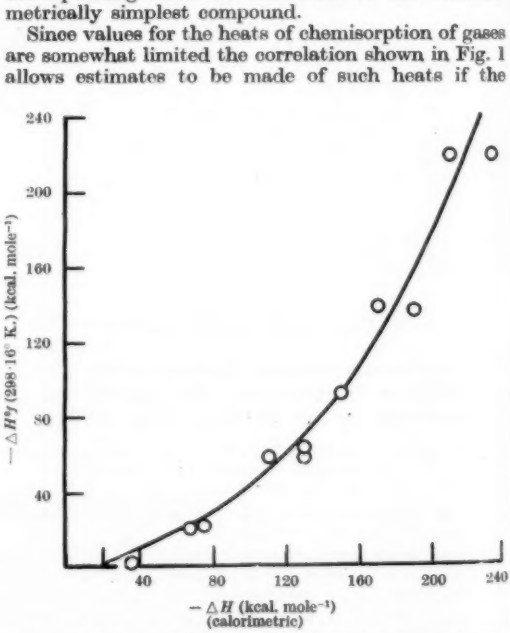

Fig. 1. Correlation between the heats of chemisorption of simple diatomic gases on metals and the heat of formation of the corresponding simple stoichiometric compounds

corresponding heat of formation is known. Recent work (Kemball, C., Wyn Roberts, M., and Saleh, J. M., unpublished results) on the sulphiding of metals has suggested that the binding energy of sulphur to nickel at − 80° C. is somewhat greater than the corresponding heat of hydrogen chemisorption (~ 35 kcal. mole^{-1}). If the chemisorbed layer simulates nickel sulphide we would expect, on the above hypothesis, a value of about 50 kcal. mole^{-1} for the heat of sulphur chemisorption since the heat of formation of nickel sulphide is − 17·5 kcal. mole^{-1}.

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Heat of Adsorption of Hydrogen on Tungsten at Elevated Temperatures

Recent work[1,2] has shown that when certain hydrides are adsorbed on tungsten filaments at low pressures, and temperatures around 1,750° K., part is apparently desorbed as a negative ion, and a residual hydrogen atom is left bound to the tungsten surface. At the low surface coverages prevailing under the conditions of experiment, the migration of these residual hydrogen atoms to adjacent sites is relatively slow, so that the process of desorption is energetically isolated from that giving rise to negative ions. The approximate strength of the tungsten–hydrogen bond formed in this process has been put at 73·5 kcal./mole (refs. 3 and 4) based on measurements at room temperature, and this value was used in deducing the mechanism outlined above, but as an order of magnitude only. Several results have now been obtained, and the argument may be inverted, to use these results in conjunction with established electron affinities and heats of atomization, to deduce the strength of the W—H bond at these elevated temperatures. Briefly, the apparent electron affinity, E', is related to the true electron affinity, E, the heat of atomization of the substrate, D, and the tungsten–hydrogen bond energy Q_r by the relation:

$$E' = E - D + Q_r$$

The values of E and D have been adjusted to a temperature of 1,750° K., the original data being taken from compilations[5,6] except for the electron affinity of oxygen, taken from Branscomb and Smith[7]. The mean value of Q_r is 73 ± 1 kcal./mole, which is practically identical with the value at lower temperatures. If there was a loss of three translational degrees of freedom of the hydrogen atom in forming the W—H bond, the bond-energy would be expected to rise by 5 kcal./mole at the higher limit of temperature, which is well outside the limits of experimental error, and the fact that the value is the same as, or slightly lower than, the room-temperature value suggests that there is a considerable degree of vibrational freedom in the adsorbed film. Two fully excited bending modes would lower the bond-energy to 72·0 kcal./mole from a value of 73·5 at room temperature, which is so close to the values obtained from the more reliable experiments with the halogen acids as to indicate that this is the true value at high temperatures. The differential heat of adsorption of molecular hydrogen on tungsten at limiting low surface coverage may readily be calculated to be 40 kcal./mole at 1,750° K., compared with 45 kcal. at room temperature.

Table 1

Substrate	E'	E	D	Q_r
Hydrochloric acid	61	93	104	72
Hydrobromic acid	70	86	88	72
Water	−32	40	221	2 × 74

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Identification of Organic Compounds by Gas Chromatography

The identification of unknown compounds separated by gas chromatography is often effected by comparison of their retention values with those of known compounds together with infra-red spectrophotometry or mass spectrometry. For this purpose graphs are prepared of log r against boiling point or log r on one stationary phase against log r on another stationary phase, where r is the retention time, relative retention time or the retention volume. Both non-polar and polar stationary phases are used to indicate the nature of the unknown substance. Wehrli and Kovats[1] have shown a relation between the structure of the substance and its retention values on two such phases. Stationary phase liquids which can take part in electron donor–electron acceptor interactions have also been used by Langer *et al.*[2] and Janak and Hrivnac[3] to separate closely similar pairs of compounds. I have also found[4] three different stationary phases to be useful in identifying components of a brown coal tar.

A method has been developed for the identification of compounds by gas chromatography alone using three stationary phases; one non-polar, one an electron donor and one an electron acceptor.

If r_1, r_2 and r_3 are the retention times (or volumes) of a substance on the three stationary phases 1, 2 and 3 under fixed conditions, we can define an 'affinity fraction' A of the substance for each phase. For phase 1 we have $A_1 = r_1/(r_1 + r_2 + r_3)$. This enables the data for a particular substance to be plotted as a point on a triangular graph.

The retention value r_b of a compound a on stationary phase b under a fixed set of conditions is proportional to $RT/(\gamma^0_a p^0_a)$, where γ^0_a is the activity coefficient of a at infinite dilution in b and p^0_a is the vapour pressure of a at column temperature. For ideal solution behaviour r_b is governed by p^0_a. In non-ideal solution the value of γ^0_a is governed by the balance of interaction energies E between like

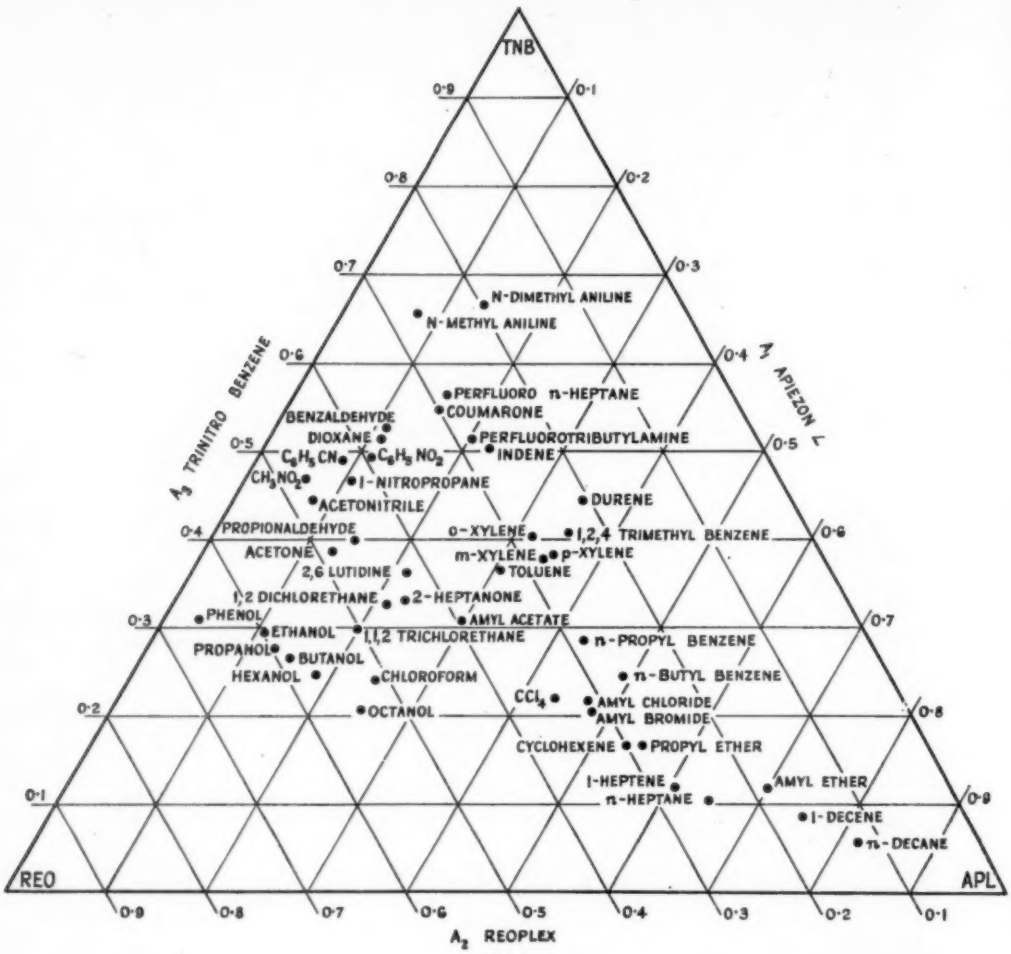

Fig. 1

and unlike molecules. For the simple case of a regular solution $\gamma^{\circ}_{a} = \exp(w/RT)$, where w is proportional to $(E_{aa} + E_{bb} - 2E_{ab})$. Thus a strong specific interaction of donor-acceptor type between the substance and the stationary phase liquid leads to a large retention value.

Retention times were measured for a number of substances at 125° C. on three 2·5-m. columns each containing 1·5 gm. of stationary phase on 9 gm. of 'Celite 545' using a nitrogen inlet pressure 1,000 mm. mercury above the outlet pressure, which was atmospheric. The A values for the substances were calculated and are shown in Fig. 1, where A_1 refers to 'Apiezon L', A_2 to 'Reoplex 400', polyester (electron donor) and A_3 to 1,3,5-trinitrobenzene (electron acceptor). Substances with low polarity have high values of A_1; $1/A_1$ is approximately proportional to the dielectric constant of the substances chromatographed. Compounds with a protonic function (electron acceptors) have high values of A_3 and substances which can act as electron donors have high values of A_2. Thus each compound has a position on the graph governed by its electron acceptor–donor properties and the group of points for each homologous series of compounds lie on a line pointing towards the 'Apiezon L' apex.

This method, together with the use of the three individual retention values, is being applied to the identification of the components of coal tar and should prove useful in the identification of the degradation products of other substances of low volatility. The method should prove useful in studying the electron donor and acceptor properties of volatile substances and of non-volatile liquids used as stationary phases. Further applications may be possible in interpreting and predicting the course of organic substitution reactions which are governed by the electron distribution in the reacting molecules.

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Some Experiments on Rice's Blue Material : Colours on Jupiter

Clarke and McTurk[1] have recently claimed that Rice's blue material can be prepared by passing ammonia through an electrical discharge tube and partially freezing out the decomposition products on a cold finger, placed about 2 cm. from the nearest electrode.

Since this observation conflicts with the results of extensive experiments carried out earlier by Rice and Freamo[2], we repeated the work of Clarke and McTurk ; but, in spite of intensive effort, we have been unable to produce the blue material from ammonia. We realize, of course, that the negative results reported in this communication, as well as those of Rice and Freamo, do not prove conclusively that the blue material cannot be formed from ammonia using the above technique, since the conditions may be very critical and difficult to duplicate.

In our experiments we used tank anhydrous ammonia as supplied by the Matheson Co. The ammonia was passed, at pressures varying from 0·1 to 2·0 mm. of mercury, through an a.c. discharge powered by a transformer rated at 10,000 V. and 50 m.amp. current. The power supply to the discharge tube could be diminished at will be means of a Variac placed between the primary coil of the transformer and the power source. The products from the discharge were partially frozen out on a cold finger at 77° K., which was about 2 cm. from the nearest electrode. In each series of experiments a discharge tube of different dimensions was used, the length being varied from 9 in. to 8 ft., the diameter from 1 to 3 cm. The electrodes were of iron except for a few experiments in which aluminium electrodes were used.

If hydrazoic acid were substituted for ammonia, we always obtained the characteristic blue deposit on the cold finger except when the current density was sufficiently high to decompose all the hydrazoic acid. Whenever this occurred, we could always obtain the blue colour by diminishing the voltage supplied to the primary of the transformer.

Since Clarke and McTurk report : "In one experiment the uncondensed gas was sampled and found by mass spectrograph to be largely hydrogen, with small amounts of nitrogen and oxygen in the ratio of 4 : 1", we assumed that air leaked into their apparatus, and that possibly nitrogen trioxide was formed ; this is blue when condensed on a surface cooled with liquid nitrogen. We, therefore, did a whole series of runs in which mixtures of ammonia and air were passed through the discharge tube, but we never succeeded in obtaining a blue deposit. We did a few experiments in which we mixed nitric oxide with small quantities (about 10 per cent) of air and passed the gas mixture, without any discharge, on to the cold finger. Under these conditions we did obtain a blue deposit of nitrogen trioxide which in colour and in its behaviour on warming could have been mistaken for the blue material. However, we never succeeded in finding any conditions under which nitrogen trioxide could be frozen out from mixtures of ammonia and air or nitrogen and water vapour on passage through a discharge tube.

These experiments on nitrogen oxides are of some importance in connexion with colours on Jupiter[3]. Recently, Kiess *et al.*[4] have shown that oxides of nitrogen are present on the atmosphere of Mars, and the suggestion has been made that the colours on Jupiter are due to frozen-out oxides of nitrogen, even though Jupiter is a 'reduced' planet. It is conceivable that non-equilibrium conditions exist on Jupiter and that the violent electrical storms might possibly result in the freezing-out of oxides of nitrogen formed by reaction of nitrogen atoms and oxygen atoms. The oxygen atoms would presumably result from the dissociation of water which may be whirled about in the turbulent Jovian atmosphere as tiny ice particles.

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BIOCHEMISTRY

Metabolism of β-Sitosterol and Other Lipids in the Presence of Acetate-2-^{14}C by Blowfly Larvæ

It has been shown recently that the ability to convert C_{28-29} sterols to cholesterol is likely to be a general attribute of phytophagous insect larvæ[1]. In the case of β-sitosterol, this conversion could occur either by removal of the side-chain and *de novo* synthesis of the cholesterol side-chain or by elimination of the supernumerary carbon atoms to yield the *iso*-octyl side-chain. Enzymes capable of cleaving the side-chain of sterols are known to occur in mammals[2] and certain bacteria[3].

Although blowfly larvæ are not as efficient in converting sitosterol into cholesterol as obligatory plant feeders, they were selected for the present work because they grow sufficiently rapidly to avoid randomization of the isotopic carbon ; they also grow readily on a synthetic diet and under aseptic conditions.

Larvæ of *Calliphora erythrocephala* were reared at 29° aseptically[4] at a density of seven animals per 10 gm. of a synthetic diet[5] in which cholesterol was replaced by purified β-sitosterol (m.p. 140° ; $[\alpha]_D$–36). Sodium acetate-2-^{14}C was diluted with carrier acetate and 2·5 mgm. added to 40 gm. of this diet, amounting to a concentration of 6·25 mgm. per cent ; the specific activity of the sodium acetate was 12 μc./mgm. The diet was continuously aerated with air free from carbon dioxide and kept in darkness during the 6 days of larval growth. At the end of this period the 27 surviving animals had attained their maximum body-weight (mean larval weight, 92 mgm.) and were used for analyses ; the radioactivity of the samples was measured with a thin end-mica window tube with an accuracy of ± 5 per cent and corrected for self-absorption in the usual manner.

The desiccated larvæ (578 mgm.) contained 19·7 per cent of ethylether – chloroform – acetone-extractable lipids, of which 83·6 per cent consisted of fatty acids and 11·5 per cent of unsaponifiable matter ; of the latter, 10·7 per cent were recovered as sterols, precipitable by digitonin. Table 1 shows the radioactivity of the various fractions. The most

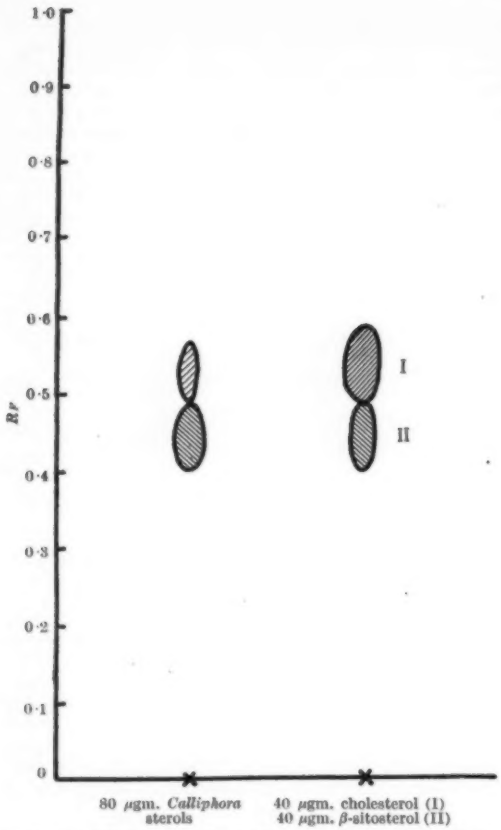

Fig. 1. Reversed-phase chromatogram of *Calliphora* sterols on Whatman paper No. 3, impregnated with 5 per cent paraffin, B.P.; ascending run for 17 hr. in ethylene glycol-mono-ethyl ether – abs. methanol – *n*-propanol – water (32 : 5 : 35 : 15 : 17·5). Chromatogram sprayed with antimony trichloride solution in chloroform and warmed for 2 min. on hot plate

striking feature is the negligible activity of the sterols. Moreover, the latter, when chromatographed on paraffin-impregnated filter paper[6] to separate the newly formed cholesterol from β-sitosterol (Fig. 1), did not show any radioactivity on X-ray films ('Kodirex'), after an exposure of 6 weeks. These findings not only confirm that *Calliphora* larvæ, like *Dermestes vulpinus*[7], are unable to synthesize sterols from ^{14}C-acetate, but indicate also that the cholesterol side-chain is not formed by re-synthesis from acetate, but rather by de-ethylation of the β-sitosterol side-chain at position C_{24}. An analogous de-methylation of ergosterol has been shown to occur in nymphs of *Blattella germanica*[8]. On the other hand, it has been claimed that adult *Periplaneta americana* incorporate ^{14}C-labelled acetate into their tissue sterols[9].

The results in Table 1 suggest that acetate is being utilized at least as efficiently for the biosynthesis of fatty acids as for the biosynthesis of the unsaponifiable matter, other than sterols; about 2·3 parts of acetate were incorporated into 1,000 parts of fatty acids. The remainder of these must be derived from other carbon sources, which in the absence of glucose in the diet[5] are obviously amino-acids. A similar observation has been made with housefly larvæ reared on a carbohydrate-free medium[4]. Adults of *Prodenia eridania* have been found to synthesize long-chain fatty acids also from acetate, which was better utilized than glucose[10].

Table 1. Distribution of Radioactivity in Blowfly Larvæ given Acetate-2-^{14}C in the Diet

Material	Radioactivity		
	Specific activity (mμc./mgm.)	Total (mμc.)	Percentage of dietary acetate-2-^{14}C
Total lipids	25·3	2,884	9·6
Unsaponifiable matter	22·4	293	1·0
Digitonin-precipitable sterols	0·3	0·4	0·001
Digitonin-non-precipitable	21·1	181	0·6
Fatty acids	27·8	2,649	8·8
Lipid-free residue	1·0	464	1·5
Total carbon dioxide expired by larvæ	—	314	1·0

Significant amounts of carbon-14 were incorporated into the unsaponifiable lipids, other than sterols; this uptake amounted to an incorporation of 1·7 parts acetate in 1,000 parts of the digitonin-non-precipitable, unsaponifiable matter. This fraction could be separated by reversed-phase paper-chromatography[6] into 4 radioactive spots, *A*—*D*, with R_F 0·65, 0·74, 0·89 and 0·97, respectively; the spots *B* and *C* were the most radioactive ones (Fig. 2). Preliminary infra-red analyses on this fraction, kindly performed by Dr. N. Sheppard, showed a spectrum of a compound with an aliphatic hydrocarbon chain, particularly of a long-chain carboxylic acid (shoulder towards 2,650 cm.$^{-1}$ due to stretching of —OH, peak at 1,707 cm.$^{-1}$ of —C=O from —COOH, shoulder at 1,415 cm.$^{-1}$ for —CH_2—[C=O], peak at 1,287 cm.$^{-1}$ with shoulders due to —C—OH of —COOH, and peak at 933 cm.$^{-1}$ due to —OH of —COOH, angle-bending

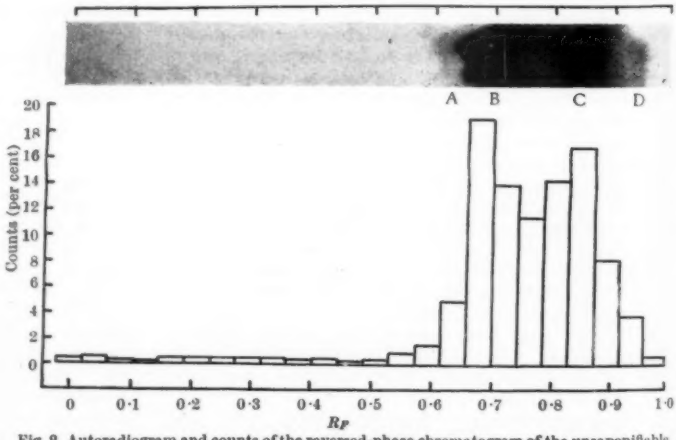

Fig. 2. Autoradiogram and counts of the reversed-phase chromatogram of the unsaponifiable, digitonin-non-precipitable matter (790 μgm.) of *Calliphora* larvæ. Whatman paper No. 3, impregnated with 5 per cent paraffin, B.P.; ascending run for 17 hr. in abs. methanol–*n*-propanol–water (80 : 15 : 5)

vibration). There was no indication of the presence of an aldehydic or keto group. Branched $—CH_3$, if any, were few (a small peak at 1,377 cm.$^{-1}$). The presence of double bonds could not be ruled out as the —C=C— frequency could have been hidden by the large —CO peak centred at 1,707 cm.$^{-1}$. Peaks at 717, 1,465, 2,850 and 2,930 cm.$^{-1}$ indicated a fair amount of CH_2 groups in an alkyl chain of considerable length. The nuclear resonance spectrum was consistent with that obtained by infra-red light; four peaks were observed (a weak one in the position of —CH=C, stronger bands due to $—CH_2—$[C=O], alkyl chain $—CH_2$ and a few terminal $—CH_3$). The ultra-violet spectrum showed ill-defined shoulders at 220 and 250 mμ.

The larvæ still contained significant amounts of radioactivity after removal of their lipids; one can therefore assume that acetate was used also for the synthesis of non-lipidic constituents of the body. The ability of *Calliphora* larvæ to incorporate ammonia into alanine, glutamic and aspartic acids[5] should be recalled in this respect.

The total barium carbonate derived from the expired carbon dioxide was 2·48 gm. for 27 surviving larvæ during 6 days. The expired carbon dioxide amounted thus to 20·5 mgm./6 days/larva or to an average of 3·2 μmoles (72 μl.) carbon dioxide/hr./larva, out of which, according to the carbon-14 count, only 1 part in 2,000 could have been derived from acetate-2-^{14}C, the rest from other carbon sources.

We wish to thank Dr. N. Sheppard for the analyses and interpretation of the infra-red and nuclear resonance spectra. One of us (Z. H. L.) wishes to acknowledge a Sir Simon Marks Fellowship awarded by the Research Council of Israel.

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Immunoelectrophoresis of Human Sera with Antiserum to Raben Growth Hormone

During investigations in progress using the immunological method for the assay of growth hormone in human serum[1,2], attempts have been made to show a reaction between human sera and rabbit antiserum to the Raben preparation of human growth hormone, made in Cambridge, in Ouchterlony plates and on electrophoretic strips.

On micro-immunoelectrophoresis in agar gel[3], human serum gave a precipitin line with the antiserum in a position corresponding with the albumen band. This line was found when normal sera and when various sera including those from acromegalic and myxœdemic patients were tested against antiserum prepared from each of four rabbits. Serum from normal non-immunized rabbits and from rabbits injected with the adjuvant mixture alone did not give this line.

Each of the four rabbits was immunized by a primary injection of 1 mgm. of Raben human growth hormone in water-in-oil emulsion ('Arlacel *A*'/'Bayol *F*') containing 200 μgm. of purified glycolipid of *Mycobacterium tuberculosis* strain 'Test', followed by a secondary injection at multiple sites six weeks later of a total of 0·5 mgm. of Raben growth hormone adsorbed to aluminium phosphate. The sera from animals bled 10 days later yielded hæmagglutination titres[2] of 1/800–1/9,600.

The line described above does not appear after absorption of the antiserum with Raben growth hormone, and evidently its formation is dependent on antibody formed against a component of Raben growth hormone. No reaction has been found against other components of human serum, such as were described by Hirschfeld *et al.*[4] using antisera to a Li and Papkoff[5] preparation of human growth hormone.

By the Ouchterlony technique, Li *et al.*[6] described reactions of identity between human growth hormone and pituitary mash put up against rabbit antiserum to growth hormone. On immunoelectrophoresis of Raben growth hormone mixed with human serum the present investigation has shown the formation of single precipitin lines against both the albumen and the Raben growth hormone bands. Identical lines were obtained on immunoelectrophoresis of human pituitary mashed in saline. Addition of human serum to the pituitary mash before immunoelectrophoresis failed to produce more than one line against the albumen band, so that the appearance of this line in the pituitary mash could be due to the contained serum. These lines clearly crossed in each of the above experiments (Fig. 1), indicating non-identity of the antigen antibody systems. In Ouchterlony plates the precipitin lines against human serum and Raben growth hormone failed to show a reaction of identity.

It is of interest that Gemzell[7] has reported biological growth hormone activity in a precipitate of human serum proteins composed mainly of albumen. Human serum albumen (kindly provided by the Lister Institute) was found to react with the four rabbit

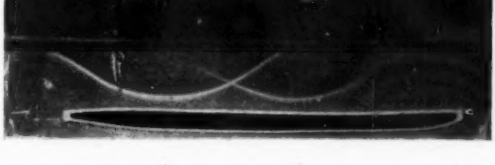

Fig. 1. Immunoelectrophoresis of human pituitary mashed in saline, with the rabbit antiserum to Raben human growth hormone, showing precipitin lines against the growth hormone (*A*) and albumen (*B*) bands, which clearly cross. Half an identical electrophoretic run is shown stained with nigrosin to demonstrate the protein bands

antisera. After absorption of the antisera with the albumen, precipitin lines still appeared against the Raben growth hormone but not against the albumen band in serum. Following pituitary destruction in two cases in which the immunological assay for growth hormone fell considerably, the precipitin line against the albumen spot cannot be demonstrated.

These results could depend on the contamination of Raben human growth hormone with human serum albumen; but these investigations have not excluded the possibility that a component of human growth hormone is carried *in vivo* on the serum albumen or that the second protein present in the Raben growth hormone is also dependent on the pituitary.

The presence of an immunologically active contaminant in the growth hormone used as antigen might invalidate an immunological method of assaying growth hormone in human serum, unless the non-specific antibody could be absorbed out, as seems possible from the experiment described above. If the reactive material in serum is considered to be growth hormone then it is so immunologically distinct from that prepared from the pituitary that the immunological assay using pituitary growth hormone as a standard may not give absolute or even comparative values for levels of growth hormone in serum.

Various investigations are in progress for the elucidation of these phenomena.

I thank Prof. C. Wilson for his encouragement and advice and Dr. R. G. White and Dr. A. Stuart Mason for much constructive guidance and criticism. The Raben preparation of human growth hormone was kindly made available by the Medical Research Council Committee on Human Growth Hormone.

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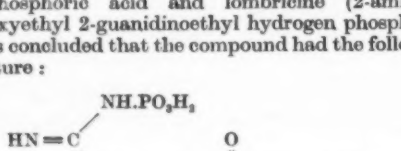
Synthesis of N-Phosphoryl-D- and L-Lombricine

The isolation of the phosphagen of the earthworm in an impure form was reported by Thoai *et al.*[1] in 1953. The compound was Sakaguchi-negative[2] and on mild acid hydrolysis yielded equimolar proportions of phosphoric acid and lombricine (2-amino-2-carboxyethyl 2-guanidinoethyl hydrogen phosphate). It was concluded that the compound had the following structure:



We have already reported[3] that the reaction of N-phosphoryl-O-methylurea[4] with 2-amino-2-carboxyethyl 2-aminoethyl hydrogen phosphate (serine ethanolamine phosphodiester) leads to the formation of a compound with properties similar to those of the substance isolated from earthworms by Thoai *et al.*[1]. The product resulting from the use of L-serine ethanolamine phosphodiester in this reaction has now been isolated by fractionation of the reaction mixture on 'Dowex-50 (H^+)' ion-exchange resin. It was obtained in 70 per cent yield as an amorphous ammonium salt, which was converted to a microcrystalline powder by recrystallization from aqueous methanol. Titration and elementary analytical data are in agreement with this material, being a mixture of the mono- and di-ammonium salts of L-2-amino-2-carboxyethyl 2-N-phosphorylguanidinoethyl hydrogen phosphate. Analysis: calculated for a mixture of 1 part of the monoammonium salt ($C_6H_{18}O_9N_4P_2.NH_4.\frac{1}{4}CH_3OH$) and 4 parts of the diammonium salt ($C_6H_{14}O_9N_4P_2.2NH_4.\frac{1}{4}CH_3OH$): C, 19·67; H, 5·94; N, 20·47; P, 15·61 per cent; found: C, 19·55; H, 5·96; N, 20·10; P, 15·54 per cent. pK_a values (potentiometric): *c.* 2, 4·6 and *c.* 8·8; as the substance was in the form of its ammonium salt the pK_a of the guanidino group could not be determined. It had main infra-red absorption peaks at 777, 969, 1,056, 1,084, 1,220, 1,309, 1,349, 1,413, 1,458, 1,628, 3,020 and 3,180 cm.$^{-1}$.

The product did not react with the Sakaguchi[5] or α-naphthol/diacetyl[6] reagent, but did react with ninhydrin and the molybdate reagent[7] for phosphate. On paper chromatography in a number of solvent systems it was homogeneous in respect to the latter two reagents. Hydrolysis in 0·1 *N* hydrochloric acid for 1 min. at 100° caused complete conversion to phosphoric acid and a guanidine base behaving as lombricine on paper chromatography. The base was further characterized as lombricine by its behaviour on nitrous acid degradation[3]. Thus, guanidination with N-phosphoryl-O-methylurea[3,4], at the terminal amino group of serine ethanolamine phosphodiester.

Direct phosphorylation of D-lombricine (isolated from earthworms) with phosphoryl chloride in strongly alkaline solution gave in 13 per cent yield a product (isolated similarly as an essentially diammonium salt) which was Sakaguchi- and α-naphthol/diacetyl-negative and had an infra-red spectrum and R_F and pK_a values identical with those found for the product described above. The isolation of natural material for comparison with the synthetic compounds is in progress.

The method of synthesis of the product obtained from serine ethanolamine phosphodiester establishes that the phosphoryl residue is located on one of the two unsubstituted nitrogen atoms of the guanidino group of lombricine; because of resonance within the zwitterionic phosphorylguanidinium group[8] these two positions are identical. That the phosphoryl residue in the product obtained by the phosphorylation of lombricine occupies a similar position is shown by the identity of the infra-red spectra of the two compounds. It may be concluded, therefore, that both products have the structure shown.

The general question of the precise location of the phosphoryl group of phosphagens derived from monoalkylguanidines, and of the identity of the natural and synthetic preparations, will be discussed at greater length in a subsequent communication. It is, however, relevant to point out here that with

the exception of the two synthetic preparations described above and the N-phosphorylglycocyamine recently synthesized by Cramer and Vollmar[10] via N-diphenylphosphoryl-S-methylurea, the accepted position for the phosphoryl residue in all these preparations—on one of the unsubstituted nitrogen atoms of the guanidino group of the parent base—although perhaps correct, remains unproved. Thus it appears that the only direct evidence in support of this formulation is based on the fact that phosphagens do not give a colour reaction with the α-naphthol/diacetyl reagent, and on the supposition[11] that N-phosphorylguanidines will show the same specificity towards this reagent as do simple alkylguanidines, of which only the mono- and *asym* di-substituted react[12]. That this supposition is unwarranted follows from an observation made in the course of the present work that phosphorylguanidine itself (prepared by the method of Cramer and Vollmar[9], or by treating N-phosphoryl-O-methylurea with aqueous ammonia) gives no colour reaction with this reagent.

With the exception noted above[10], previous syntheses of phosphagens derived from monoalkylguanidines have invariably involved the reaction of phosphoryl chloride with the guanidine base in a strongly alkaline medium. It would seem likely, by analogy with the structure of the phosphorylation product of lombricine, that the phospboryl group of these products is, indeed, in the accepted position, that is, on one of the unsubstituted nitrogen atoms of the guanidino group of the parent base. Although these synthetic preparations have been claimed[11] to be identical with the natural, there seems insufficient evidence available at present to warrant any definite conclusion on this point.

These questions are now under investigation and the results, together with a complete account of the present work, will be published elsewhere, but already from the work reported here, the potential value of the synthetic method involving N-phosphoryl-O-methylurea and its derivatives in orientating the phosphoryl residue throughout this group of naturally occurring compounds is clear.

We are indebted to Dr. J. E. Fildes and staff, to Dr. E. Spinner and Mr. D. T. Light, and to Dr. D. Perrin and Mr. H. Satrapa, of the Department of Medical Chemistry, for microanalyses, infra-red spectra and pK_a determinations, respectively.

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Synthesis of Thiamine and Folic Acid by *Nocardia rhodnii*, the Micro-symbiont of *Rhodnius prolixus*

Strong suggestive evidence[1] exists to support earlier proposals[2] that *Nocardia rhodnii*, the extracellular symbiont of *Rhodnius*, contributes essential food factors to its host. In recent years, however, the evidence has been conflicting, particularly where it concerns the nature of these factors. In 1954, Geigy, Halff and Kocher[3] isolated a micro-organism from *Triatoma infestans* similar to *N. rhodnii* and found that whereas it synthesized thiamine and other vitamins in minimal amounts, there was a 2,500-fold hyper-production of folic acid. Bewig and Schwartz[4], however, later claimed that this organism was not *N. rhodnii*, and was not symbiotic. They showed that pure cultures of *N. rhodnii* on an elaborate semi-synthetic medium synthesized minimal amounts of folic acid, no vitamin B_{12} and no folininic acid. They found too that injection of vitamins into sterile *Rhodnius* failed to induce moulting. In 1956 Baines[5], using feeding and injection techniques, came to the conclusion that *Rhodnius* is dependent on *N. rhodnii* for pyridoxine, calcium pantothenate, nicotinamide and thiamine, but that biotin and folic acid are present in adequate concentration in the host blood to meet the requirements of *Rhodnius*.

The two experiments described here attempt to throw further light on the synthesis of folic acid and thiamine by *N. rhodnii* and *Rhodnius*. Techniques involving the injection of vitamins into insect or mammalian host were avoided. In the first experiment, the vitamins were fed artificially to sterile bugs using my technique[6], and in the second the synthesis of the two vitamins by *N. rhodnii* was determined microbiologically[7].

Exp. 1. The effect of rabbit blood supplemented with folic acid and/or thiamine, as a diet for sterile 4th instar *Rhodnius*.

Sterile insects do not respond well to artificial feeding, and only small volumes of blood are usually ingested. This difficulty was overcome by adding the test vitamins to oxalated horse blood in such concentrations that the small amount of blood taken in would contain approximately the quantity of vitamins required for the experiment. The weight of blood ingested, and hence the amount of vitamin, was determined by rapidly weighing the bugs before

Table 1. Effect of Folic Acid and/or Thiamine on the Moulting of Sterile 4th Instar *Rhodnius* fed on Small Amounts of Horse Blood containing the Vitamins, followed by Capacity Meals on the Rabbit Ear

Group	Diet	No. used	Mean amount of vitamins introduced (μgm.)	Effect
A	(Horse blood) + full feed on rabbit	8	—	No moults in 70 days
B	(Horse blood + folic acid) + full feed on rabbit	2	0·035	No moults in 70 days
C	(Horse blood + thiamine) + full feed on rabbit	2	0·18	Both moulted in 41 and 53 days
D	(Horse blood + folic acid + thiamine) + full feed on rabbit	2	0·02 folic acid 0·075 thiamine	Both moulted in 15 and 26 days
E	Full feed on rabbit (normal, infected bugs)	98	—	Mean moult period: 15·5 days

and after feeding. The amount of blood ingested represented about 25 per cent of a capacity blood meal. After weighing, the bugs were placed on the ear of a rabbit when they fed to repletion. The results show that the amount of horse blood introduced into the bugs before the rabbit feed does not affect the time of moulting of the experimental insects.

The results analysed statistically show that the delay in groups *A* and *B* compared with the control, *E*, is readily apparent. It is also significant, in the main, for group *C*; for group *D*, any delay in moulting must remain in doubt. It also seems apparent that folic acid and thiamine together have a far more significant effect than either vitamin alone.

Exp. 2. Quantitative microbiological estimations of thiamine and folic acid synthesis by *N. rhodnii* in sterile horse blood.

Pure cultures of *N. rhodnii* were isolated from infected bugs and kept at 30° on nutrient agar slopes. Microscopical examination did not show any accompanying organisms. Sterile horse blood was chosen as the culture medium as blood is the natural substrate of *N. rhodnii* in the *Rhodnius* gut. 1 day before the commencement of the experiment, a sub-culture from the original agar slopes was transferred to a liver peptone broth and incubated at 30°. On the first day the culture from this broth was washed with, and suspended in, isotonic saline. Three drops of this pure culture in suspension were used as the inoculum, and were added to two of three tubes of 5 ml. freshly drawn, sterile horse blood. The third sample of blood was not inoculated and served as the control.

Levels of thiamine and folic acid in control and inoculated groups were determined at the beginning of the experiment and after 3 and 7 days (Table 2).

Table 2. VITAMIN SYNTHESIS BY *N. rhodnii* IN HORSE BLOOD
(Values expressed as mγ/ml.)

Time in days after inoculation	Thiamine		Folic acid	
	Normal blood control	Inoculated blood	Normal blood control	Inoculated blood
First	36	—	28	—
Third	33	35	32	71
Seventh	41	96	29	122
	37 (mean)	—	30 (mean)	—

The results show that by the seventh day there is a 2·6-fold increase in the thiamine-level in the inoculated blood over that in pure, *Nocardia*-free blood, and a 4-fold increase of folic acid. Using Bewig and Schwartz's figure[8] for the folic acid requirements of *N. rhodnii* as 0·1 mγ/cm.³, it can be seen that in the present experiments this organism produces about 920 times its own requirements of folic acid. Without knowing the thiamine requirements of the organism, it is not yet possible to determine what excess of this vitamin is produced.

It therefore seems likely that both folic acid and thiamine are synthesized by *N. rhodnii* in such amounts that the excess over the organism's own requirements could be made available to its host for its satisfactory growth and development.

This work forms part of a study for the degree of Ph.D. of the University of London, and was carried out under the late Prof. P. A. Buxton, whose helpful criticisms, together with those of the present head of the Department, Prof. D. S. Bertram, I much appreciate. It was financed by the South African Council for Scientific and Industrial Research, the support of which I wish to acknowledge.

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Effect of Degeneration on the 'Albumin' Components of Human Muscle Extracts

JACOB[1] showed that a fast-moving group of proteins, which he called group III, was observed when low ionic strength extracts of rabbit striated muscle were subjected to moving boundary electrophoresis. The group consisted of a major and a minor component; the major component, unlike the minor, was soluble in distilled water and he considered that it probably corresponded to the myoalbumin described by Bate-Smith[2]. Subsequent reports[3–5] have claimed that this group increases relative to other proteins in the muscle extracts when the striated muscle of various species, including man, degenerates as a result of pathological and experimental lesions. The increase has been attributed to an increase of myoalbumin. Recently, Corsi and Buscaino[6] have pointed out that much of the group III fraction is likely to consist of serum albumin. However, since the electrophoretic techniques used previously appear to have resolved only one albumin component, interpretation of the results is ambiguous. In view of this the following preliminary observations may be of interest.

I have recently described[7] the use of starch-gel electrophoresis by Smithies's method[8] for the separation of the human muscle proteins which are soluble at low ionic strength. At that time the occasional separation of the albumin fraction into two components was reported; in this context, by the albumin fraction is meant the fastest-moving fraction seen after starch-gel electrophoresis and which has albumin-like solubility characteristics. When separation occurred the slower component moved at the same speed as serum albumin. Further investigation has defined the conditions under which the albumin fraction of muscle extracts can be invariably separated into two components. Both components, like the major component of Jacob's group III, are soluble in ion-free water. Although the relative amounts of the two components vary considerably, some peroxidase activity is always associated with the faster component, but not with the slower under the conditions of the present experiments. The significance of this observation is as yet unknown, and it is included merely as indicating a

dissimilarity, other than in electrophoretic mobility, between serum albumin and the muscle protein.

The factors influencing the speed of migration of proteins on starch may be rather complex[8]; nevertheless, the relative mobilities are such as to suggest that the faster component may be myoalbumin, since Bate-Smith[2] showed that this had a lower isoelectric point than the corresponding serum albumin.

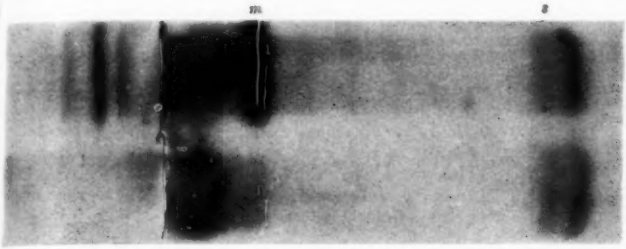

Fig. 1. Starch electropherogram of two muscle extracts run in parallel: *A*, Normal muscle; *B*, atrophied muscle. Buffer, 0·03 *M tris*-(hydroxymethyl) amino methane/hydrochloric acid, *p*H 7·7. *m*, Myoglobin; *s*, serum albumin

Fig. 1 is a photograph of a starch-gel electropherogram in which low ionic-strength extracts of a normal (*A*) and an atrophied human muscle (*B*) have been run side by side. Atrophy in this case had resulted from severe chronic denervation. Several components, for example the myoglobin band, have largely disappeared from the electropherogram of the atrophied muscle; but the bands due to the albumin components are of similar intensity in the two cases and hence these components are proportionately increased. Although the relative amounts of the two albumins are not always quite the same as in the example shown, nevertheless, when muscle degeneration is accompanied by a marked reduction in the intensity of certain characteristic bands on the starch electropherogram, no obvious reduction in the intensity of either albumin band occurs. The proportionate increase in serum albumin probably reflects a decrease in the intracellular space relative to the extra-cellular space resulting from destruction of muscle cells. On the other hand, the increase in the faster component, which may be human myoalbumin, is understandable if it represents, as Fischer[3] has suggested, a breakdown product of other muscle proteins.

This work, which is continuing and will be reported in detail elsewhere, was supported by a research fellowship of the Mason (Chiswick) Medical Research Trust.

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Characterization of Deoxyribonucleic Acid from *Anacystis nidulans*

The chemical nature of deoxyribonucleic acid in blue-green algæ was not known until very recently[1–3]. This communication deals with a quantitative study of deoxyribonucleic acid from *Anacystis nidulans* and its characterization in respect to that from other sources. *Anacystis nidulans* and *Chlorella ellipsoidea* were grown in continuous culture chambers as described earlier[4,5]. The algal cells were treated with cold 10 per cent trichloracetic acid, 95 per cent alcohol, alcohol/ether (3 : 1) and finally with ether until all the pigments except phycobilins were fully extracted. Deoxyribonucleic acid was isolated by one of the following procedures: (*a*) with 10 per cent sodium chloride (2 ml./10 mgm.) three times by refluxing at 80° C. for 1 hr. each time[6]; (*b*) with 1 *N* potassium hydroxide at room temperature[7]; (*c*) with 0·5 *M* perchloric acid[8]. Purification of deoxyribonucleic acid from protein and polysaccharide was done according to the methods described earlier[9]. Chromatographic analyses were done according to Wyatt[10]. Purines and pyrimidines were estimated by maximum extinction technique[11]. With different procedures of extraction it has been observed that the yield of purified deoxyribonucleic acid varies from 3·7 to 4·7 per cent of the dried cells after ether wash. The fresh weight of the cells was found to be 5 times that of the dried ether-washed cells and hence deoxyribonucleic acid constitutes 0·73–0·94 per cent of the fresh weight of the cells. Nitrogen content varies from 13·9 to 14·3 per cent and that of phosphorus from 6·8 to 8·2 per cent with different procedures of isolation. Deoxyribonucleic acid is found to have an absorption maximum at 257 mμ and minimum at 230 mμ. The infra-red spectrum of deoxyribonucleic acid from *Anacystis* does not show any remarkable deviations from those of other sources. The main peaks are at 3, 6·1, 8·1 and 9·3–9·8μ. The percentage of molar ratios of constituent bases, guanine, adenine, cytosine and thymine, in deoxyribonucleic acid of *Anacystis* was found to be 29·5, 23·3, 24·8, and 22·3 respectively. The ratios of G/C, A/T and Pu/Py were 1·19, 1·04 and 1·12 respectively. The average values only have been recorded here. The deviation of unity in base ratio in this case is very difficult to explain at present, though the presence of single-stranded deoxyribonucleic acid which has recently been isolated from bacteriophage[12] cannot be ruled out. The (A + T)/(G + C) ratio may be used as a species parameter. In the case of *Anacystis nidulans* this was found to be about 0·82.

The deoxyribonucleic acid from *Anacystis nidulans*, *Chlorella ellipsoidea* and sperm (obtained from Nutritional Biochemical Corporation, Cleveland, Ohio) was degraded with deoxyribonuclease in the following way. 48 mgm. deoxyribonucleic acid, 1·28 mgm. deoxyribonuclease in 0·003 *M* magnesium sulphate and 0·02 *M* phosphate buffer *p*H 7·6, total volume being 4·8 ml., was incubated at 37° C. for 24 hr. The deoxyribonuclease hydrolysate was chromatographed in *iso*propanol/water (7 : 3) with ammonia in vapour phase[13]. The incubation of

Table 1. Molar Proportions of Bases in the First Band after Chromatographic Separation of Deoxyribonuclease Hydrolysate and in the Core after 24 hr. of Deoxyribonuclease Treatment and Dialysis

	Source	G	A	C	T	G/C	A/T	Pu/Py
First band	*Anacystis nidulans*	32·5	23·5	25·5	18·5	1·27	1·27	1·27
Core, 18–20 per cent	*Anacystis nidulans*	33·5	23·2	24·5	18·7	1·37	1·24	1·31
First band	*Chlorella ellipsoidea*	33·0	22·0	23·0	22·0	1·50	1·00	1·22
Core, 18–20 per cent	*Chlorella ellipsoidea*	32·6	23·5	22·5	21·4	1·44	1·10	1·28
First band	Sperm	20·5	36·0	15·5	28·0	1·32	1·28	1·30
Core, 34–40 per cent	Sperm	20·8	39·2	17·6	22·4	1·18	1·75	1·50

First band of deoxyribonuclease hydrolysate after chromatographic separation (*iso*propanol–water, ammonium) was eluted in 0·1 *N* hydrochloric acid, hydrolysed with 12 *N* perchloric acid and the proportion of bases was determined spectrophotometrically. The methylcytosine in the case of sperm deoxyribonucleic acid was not detected after perchloric acid hydrolysis. Core signifies the non-dialysable fraction when digestion was carried out in dialysis tubes against 500 ml. of distilled water. 48 mgm. of deoxyribonucleic acid was used.

Table 2. Electrophoretic Separation of Chromatographic Band 3 of the Deoxyribonuclease Hydrolysate

Spot No.	Electrophoretic mobility (cm.)	Identity	Source
1	0	pC	*Anacystis*, *Chlorella*, sperm
2	2·5–3·5	pApC	*Anacystis*, *Chlorella*, sperm
3	4·5–5·5	pGpC	*Anacystis*, *Chlorella*, sperm
4	6·5–7·0	pApG	*Anacystis*, sperm
5	12·0–14·0	pT	Sperm

Electrophoresis was carried out at 4° C. in citrate buffer *p*H 3·5 and voltage gradient 15 V./cm. for 2 hr. pC, deoxycytidylic acid; pApC, dinucleotide of deoxyadenylic and deoxycytidylic acids; others are similarly assigned. No sequence of nucleotides is indicated in the case of dinucleotides. The ratio of two bases in the case of dinucleotides was found to be approximately unity.

deoxyribonucleic acid with deoxyribonuclease in the dialysis tube showed that the core, that is, non-dialysable fraction in the case of sperm deoxyribonucleic acid, contains 36–40 per cent of the original deoxyribonucleic acid whereas in the case of *Anacystis* and *Chlorella* it is only 18–20 per cent. In separate experiments deoxyribonucleic acid was incubated with deoxyribonuclease similarly without dialysis and the hydrolysate was chromatographed[12]. Three distinct bands were detected under ultra-violet light and those were designated as band 1, 2, 3 according to their higher migration in the chromatogram. The first band was analysed after elution with 0·1 *N* hydrochloric acid. Molar proportion of bases in the first chromatographic band of hydrolysate and in the core is given in Table 1. In all the samples the ratio of purine to pyrimidine is higher both in the first band and the core. The third chromatographic band was subjected to electrophoresis[13] in citrate buffer *p*H 3·5 and voltage gradient 15 V./cm. for 2 hr. using Spinco paper electrophoresis apparatus. It was observed that the third band after electrophoresis was separated into four spots in the case of *Anacystis*, three spots in the case of *Chlorella* and five spots in the case of sperm. The spots were designated as 1, 2, 3, 4 and 5 according to their higher electrophoretic mobilities. The electrophoretic mobilities of the spots and their probable identities are given in Table 2. Spot 4, which has been identified as dinucleotide of deoxy-adenylic and deoxy-guanylic acids, is absent in the case of *Chlorella*, indicating the occurrence of less adenine guanine linkage than that in *Anacystis* or sperm deoxyribonucleic acid. From this point of view sperm deoxyribonucleic acid differs from that of *Anacystis* in containing a distinct thymidylic acid spot in the third band. In short, it appears that the deoxyribonucleic acid of *Anacystis nidulans* contains more adenine–guanine linkages than that of *Chlorella ellipsoidea* and fewer thymidylic acid units than that of sperm. The analyses of other portions of deoxyribonucleic acid may reveal more differences in the arrangement of the nucleotides in deoxyribonucleic acid of blue-green algae from those of other sources which have chemically identical composition.

Details of this work will be published elsewhere.

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RADIOBIOLOGY

In vitro Uptake of Iodine-131 by Tissues of Rainbow Trout

Recently, it has been shown that *in vitro* uptake of iodine-131 by the lactating mammary tissue of rat was 10–15 times that of liver, muscle or boiled mammary tissue. Further, the data on the *in vitro* uptake of iodine-131 by different tissues of rat indicate that iodide concentration mechanism in the mammary, salivary and gastric glands but not in liver or placenta appears to be similar to that of thyroid gland in the rat[1]. In the case of fish, it has been shown that the thyroid hormone is not involved in the regulation of oxidative metabolism, and thus it was decided to study the *in vitro* uptake of iodine-131 by different tissues of rainbow trout (*Salmo gairdnerii*)[2]. Tissue slices from one-year-old rainbow trout were incubated for 2 hr. at 13° C. in flasks containing 2 ml. Nandi and Bern medium[4]. The *T*/*M* values (counts per min. per 100 ml. tissue divided by counts per min. per 0·1 ml. medium) for different tissues were calculated.

The values of the ratio T/M for *in vitro* uptake of iodine-131 by different tissues of rainbow trout indicated that only thyroid follicles present in the lower jaw concentrated iodine-131. The T/M value was higher in the case of the posterior part of the lower jaw than the anterior part, indicating that the thyroid follicles are comparatively more numerous in the posterior part. Uptake of iodine-131 was higher in the lower part of the gill than the upper part and this may be due to the presence of some thyroid follicles at the base of the gills where they are attached to the lower jaw. Addition of thiouracil (0·02 mgm./ml.) to the medium did not affect uptake of iodine-131 by thyroid follicles, whereas potassium thiocyanate blocked such uptake by thyroid follicles. The T/M values for uptake of iodine-131 by different organs of the digestive system, kidney, head kidney, liver, spleen, heart muscle, skeletal muscle or brain were less than 1·0, indicating that these organs or tissues have a relatively poor ability to concentrate iodide *in vitro*.

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PHYSIOLOGY

Protein and Lipid Content of *Chlorella vulgaris* in Relation to Light

Incidental to other work, we have observed an effect of light on *Chlorella vulgaris* which can be interpreted as indicating an influence of different spectral regions on the synthesis of protein and lipid.

A strain of *Chlorella vulgaris* which has been maintained in this laboratory since 1938 was cultured in an inorganic medium consisting of potassium nitrate, 0·025 M; crystalline magnesium sulphate, 0·02 M; potassium dihydrogen phosphate, 0·018 M; crystalline ferrous sulphate, 0·00005 M; and potassium citrate, 0·00005 M. Air, enriched with 5 per cent carbon dioxide, was bubbled through the culture solutions continuously. Duplicate sets of flasks, with an initial population of 100 cells/mm.^{3}, were illuminated continuously at a total incident radiation of 600 foot candles, as measured with a Weston illumination meter, model 603. Illumination for one set was provided by daylight fluorescent lamps and for the other set by tungsten filament lamps.

The wave-length distribution of the radiation was such that, although both sets of cultures received equal total amounts of incident visible radiation, the 'filament' cultures received one-half as much radiation as the 'fluorescent' cultures in the 440–455 mμ region of the spectrum (60 f.c. vs. 120 f.c.) and twenty times as much radiation in the 655–700 mμ region (71 f.c. vs. 3·55 f.c.). Despite the differences in the ratio of red to blue intensities incident on cultures under these light sources (1·18 for the 'filament' and 0·029 for the 'fluorescent'), the total incident radiation in the two regions combined was about the same for both sets of cultures (131 foot candles for the 'filament' and 123·55 for the 'fluorescent').

All cultures were maintained at 23 ± 1° C.

Cell counts were made in duplicate for each culture at approximately 24-hr. intervals by means of a hæmocytometer. Total packed volumes and dry weights were determined in the conventional ways at the end of each experiment (15 days). Total nitrogen and total protein were determined as described by Umbreit[1] and total lipid was determined by the method of Stekol *et al.*[2].

Table 1 shows that the final population achieved, total packed volume, and proteins formed were substantially greater in cultures exposed to the filament source than in those exposed to the fluorescent source. However, the yield of lipid (expressed as per cent of dry weight) was lower in the 'filament' than in the 'fluorescent' cultures. But, despite the difference in percentage yield of lipid, the yield in absolute terms was about 3·4 times greater in the 'filament' cultures because of the greater total growth (2·28 mgm. of lipid/ml. of culture versus 0·67 mgm./ml. of culture).

Table 1. Relation of Certain Cell Characteristics to Light Source in *Chlorella vulgaris*

Characteristic (15-day culture)	Light source		Filament
	Filament	Fluorescent	Fluorescent
Population (cells/mm.^{3})	100,070	70,000	1·43
Packed volume (mm.^{3}/ml.)	14·50	9·00	1·61
Dry weight (mgm./ml. of culture)	10·31	2·31	4·46
Total protein (per cent of dry weight)	49·86 ± 5·23	39·64 ± 5·41	1·26
Total lipid (per cent of dry weight)	22·2 ± 2·89	29·0 ± 1·82	0·76
Total carbohydrate (by difference)	26·48	25·55	1·04

The differences in protein and lipid contents of cells grown under the two different light sources are clearly significant within 95 per cent confidence limits. The critical ratio of protein from 'filament' versus 'fluorescent' cultures was 4·48 (t 0·05 = 2·086). The corresponding value for lipid content was 3·96 (t 0·05 = 2·048).

Peaks in photosynthetic efficiency occur in the 440–455 mμ and in the 650–700 mμ regions[3]; but what effect, if any, these wave-lengths may have on subsequent biochemical conversion of the primary products of photosynthesis is not known. The present experiments show that, with the light sources and total radiation employed, the relative protein content is higher and lipid content is lower in *Chlorella vulgaris* cultured under light conditions relatively deficient in the 440–455 mμ region and distinctly richer in the 650–700 mμ region (filament source) than in cells exposed to a light source that is rich in the blue wave-lengths and relatively deficient in the longer wave-lengths. However, the experiments do not indicate which of these regions is more important in determining the protein and lipid contents and the protein/lipid ratio in the cells or whether the determining factor is the ratio of blue to the longer wave-lengths or, indeed, whether other wave-lengths have an important role. These facets of the problem are being investigated.

Two-dimensional paper chromatography showed no qualitative difference in the amino-acid content of

protein from 'filament' and 'fluorescent' cultures. Alanine, arginine, aspartic acid, glutamic acid, glycine, *iso*leucine, leucine, serine, threonine, and valine were identified in the protein from both sources.

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Interaction between Repetitive Nerve Stimulation and Twitch-potentiating Agents at the Neuromuscular Junction

THE indirectly developed maximal twitch tension of vertebrate muscle is sometimes augmented after periods of tetanic nerve stimulation, an effect generally called post-tetanic potentiation. This effect is further increased by the administration, prior to tetanic conditioning, of physostigmine in doses which in themselves are too small to facilitate twitch tension[1]. Physostigmine[2] and also other agents which elicit twitch potentiation, for example neostigmine[3] and *m*-hydroxy phenyltrialkylammonium ions[4], have been shown to possess an action on motor nerve terminals which is revealed by bursts of repetitive antidromic nerve discharge appearing after single orthodromic volleys. Furthermore, this presynaptic activity is greatly facilitated by tetanic conditioning of the motor nerve[5]. Within the context of these observations, it seemed important to compare drug-induced twitch potentiation before and after periods of repetitive motor nerve stimulation.

Drugs dissolved in isotonic saline were injected into the arterial supply of the cat gastrocnemius muscle before and at different intervals after a 10–20 sec. period of motor nerve stimulation at frequencies of 50–400/sec. Except for these periods of tetanic conditioning, the nerve was stimulated by single supramaximal shocks at a rate of 1 every 6 sec. Antidromic nerve discharge was displayed on a cathode-ray oscilloscope. A monopolar recording electrode was placed on an *L*7 ventral root filament and an indifferent electrode on the skin. All cats were anæsthetized with chloralose. Two groups of drugs were used as test agents. Group I comprises *m*-hydroxy and *p*-hydroxy phenyltrialkylammonium ions and neostigmine; Group II consists of phenyltrialkylammonium ions and a variety of aliphatic quaternary ammonium ions including tetraethylammonium. A characteristic feature of Group I agents is the perfect correlation exhibited between their twitch-potentiating potencies (on single shock stimulation) and *in vitro* anticholinesterase activities[6]. The Group II compounds lack such a correlation and most of them are relatively much weaker than the other agents as either twitch potentiators or cholinesterase inhibitors. In contrast to Group I agents, the compounds of Group II rarely elicited post-activation antidromic motor nerve discharges; they did, however, regularly produce this neural response after 10-sec. periods of tetanic conditioning (200 per sec.) or on stimulation every 7 sec. with paired shocks separated by 1–3 msec., conditions which also facilitate the post-activation neural response to Group I agents[5].

In twenty nerve-muscle preparations, consistent results were obtained when agents of Group I and Group II were injected after periods of tetanic stimulation: drug-induced twitch potentiation greatly exceeded that obtained in response to equal, or smaller, doses administered prior to the tetanic conditioning. A characteristic result is illustrated in Fig. 1. Repeated administration of a test dose at different intervals after tetanic conditioning permitted determination of time course and duration of the post-tetanic enhancement of pharmacological response. Using *m*-hydroxy phenyldiethylmethylammonium and its non-hydroxy analogue as test agents, enhancement of drug-induced twitch potentiation in 8 different nerve-muscle preparations endured for 10–80 min. after one conditioning tetanus (200/sec. for 20 sec.). In 5 of these preparations, the time of return to pre-tetanic drug response exceeded 20 min. The maximal pharmacological effect was always produced by the first post-tetanic injection of drug, usually made within 30 sec. after cessation of the tetanus. From then on, the effect decayed in an

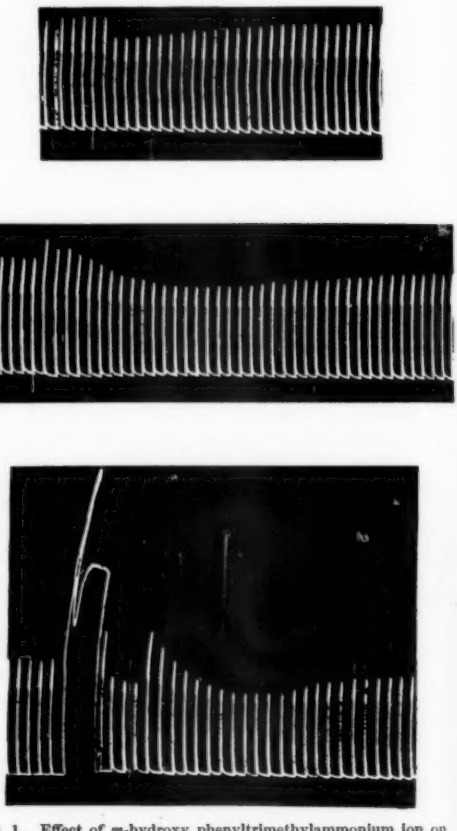

Fig. 1. Effect of *m*-hydroxy phenyltrimethylammonium ion on isometric twitch tension before and after tetanic conditioning. Chloralosed cat. Single maximal shocks applied to posterior tibial nerve every 6 sec. as square waves of 0·5 msec. duration; marks at bottom of trace indicate time of injection. Top, Response to test agent, 1 μgm./kgm. intra-arterially; middle, response to test agent, 5 μgm./kgm. intra-arterially; bottom, response to test agent, 1 μgm./kgm. intra-arterially after tetanic nerve stimulation at 300 sec. for 20 sec. Note that injection was made during a post-tetanic depression of twitch tension

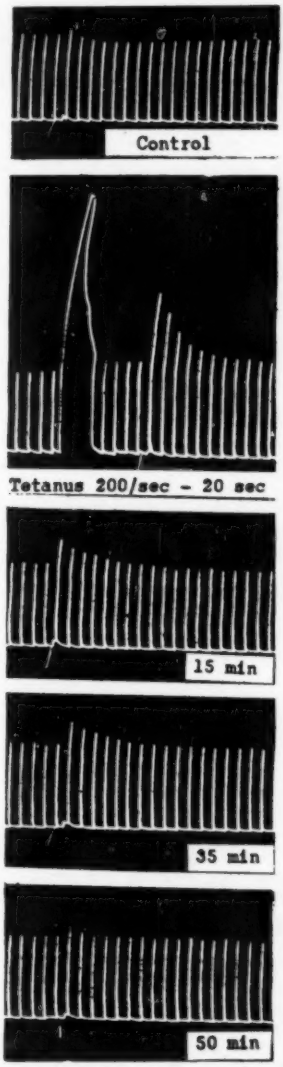

Fig. 2. Effect of phenyldiethylmethylammonium ion on isometric twitch tension before and at various intervals after tetanic conditioning. See legend to Fig. 1 for technical details. All injections were 50 μgm./kgm. intra-arterially. Note that first injection of test agent after tetanus (20 sec.) was given during post-tetanic potentiation of twitch tension. Not shown here is response to test agent 75 min. after tetanus; this response was same as shown in top tracing

exponential manner until the pre-tetanic level of response was attained (Fig. 2).

This increase in pharmacological response produced by tetanic conditioning was observed irrespective of whether the post-tetanic twitch tension in the absence of drug was potentiated, depressed or unchanged relative to pre-tetanic tension. This increase is, therefore, not contingent on the selection of stimulus parameters which result in post-tetanic potentiation *per se*.

The duration of enhanced drug-induced twitch potentiation observed after tetanic conditioning is considerably longer than that of other post-tetanic phenomena previously studied: decurarization[7,8], increase in miniature potential discharge-rate[9], twitch potentiation[1]. These latter events, subsiding within 5–10 min. at the most, have been attributed to an action on presynaptic terminals which augments transmitter output[8,9]. The increased drug-induced twitch potentiation seen after repetitive nerve stimulation also appears to have a presynaptic origin; this suggestion is supported by the finding that twitch-potentiating compounds, including those which are not cholinesterase inhibitors, produce a post-activation antidromic motor nerve discharge which is markedly facilitated in frequency and duration by tetanic conditioning. Perhaps the post-tetanic increase in pharmacological response constitutes a more sensitive measure of the duration of presynaptic changes consequent to repetitive nerve stimulation than is provided by changes in miniature potential discharge-rate, post-tetanic decurarization and twitch amplitude. Alternatively, the post-tetanic increase in drug-induced twitch potentiation may result from changes in neuromuscular transmission which are unrelated to these other more transient post-tetanic phenomena.

In the absence of further information concerning the nature of the presynaptic alterations involved, we may conclude that the effects of repetitive nerve stimulation and of twitch-potentiating compounds on presynaptic terminals are interchangeable and additive.

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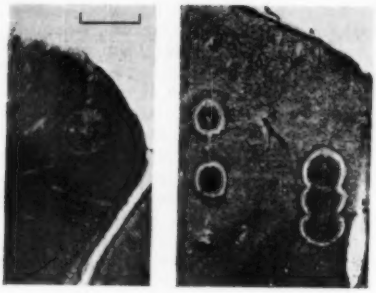
Locating Capillary Microelectrode Tips within Nervous Tissue

FOR the identification of structures generating potentials recorded by micropipettes it is necessary to locate the position of the micropipette in the tissue. The method most frequently used to obtain this information consists in depositing a marker at the tip of the micropipette. Most authors employ an electrolyte of good conductivity the composition of which does not disturb the functions of the cells but which leaves a trace when a small amount of it is extruded from the electrode by electrophoresis. Thus, crystal violet in hydrochloric acid[1], lithium carmine in potassium chloride[2], silver nitrate[3] and potassium ferrocyanide[4,5] have been used for markings in the retina, whereas gold trichloride in potassium chloride (von Baumgarten, R., personal communication) and ferrous ammonium sulphate[6] were used



A *B*

Fig. 1. Frozen sections. 100μ, according to the plan of the penetrating electrode. Hæmatoxylin–eosin stain. *A*, Single mark in cat cortex (suprasylvian gyrus); *B*, multiple marks in pigeon telencephalon; left, two sites of marking at 1 mm. distance; right, three sites at 0·5 mm. Index: 1 mm.

for the central nervous system. To our knowledge, none of these methods is used routinely. This is probably due to the irregularity of the results and also to the difficulty of finding the very small mark left in the tissue.

To obviate the above-mentioned difficulties, we have devised a method in which the extruded marking ions are complex anions containing copper and citrate. The advantage of complexing the copper is that a too drastic fixation of copper on to the proteins of the nervous tissue is thereby avoided. It is well known that if a solution of a simple salt of a heavy metal is used as an electrolyte, the release of metal cations provokes a considerable and almost immediate increase in the electrode impedance. This inhibits the current-flow, and, in most cases, the result is that the coagulated proteins adhere to the tip of the micropipette, so that it is impossible to remove the micropipette without removing at the same time the marking deposit. If, however, the copper is complexed, the impedance of the electrode remains constant during the entire time of current-flow and the tip of the electrode remains clean, no coagulum being seen on inspection under the microscope.

In practice we use an electrolyte containing complex anions of copper and citrate, obtained by dissolving 811 gm. (2·5 moles) of tripotassium citrate monohydrate and 213 gm. (1·25 moles) of cupric chloride dihydrate in 1 litre of water and adjusting the *p*H to 7 with the necessary amount of strong potassium hydroxide solution. In the 0·5, 1·5μ micropipettes (4–40 MΩ) this solution can be conveniently substituted for the electrolytes (potassium chloride, sodium chloride) generally used for the detection of spikes. (We are grateful to Prof. P. Souchay (Department of Chemistry, Sorbonne, Paris) for his advice on the preparation of complex ions.)

After recording, the marking is obtained by passing a continuous 2-μamp. current with microelectrode negative, for 2 min. The specimen is then fixed in 10 per cent neutral formol and embedded in paraffin (or sliced frozen). Nissl or panoramic staining is then carried out by the usual techniques. The method was tested on pigeon and cat brains. In both cases, after staining the tissue, a well-defined, colourless ring appears, having a diameter varying with the preparation from 300μ to 800μ. Examination of serial sections shows that this ring results from the cutting of a sphere (or ellipsoid), the centre of which is the tip of the electrode. When the section passes through a diametrical plane, a colourless spot having a diameter of 50–100μ likewise appears in the centre of the ring. An examination at higher magnification shows that the absence of staining in the ring and in the centre corresponds to tissue lysis, due probably to denaturation of the proteins by the copper. This assumption is supported by the fact that perfusion with an acidified Ringer solution before killing the animal prevents the formation of the ring whereas an alkaline perfusion favours it. It is known that metal-protein bonding is facilitated by an increase in *p*H. We think that the formation of the ring around the central point is due to a passive diffusion of the product after its release from the tip of the electrode, since the intensity of the current and the time of its application have little influence on the diameter of the sphere.

It seems to us that this method is likely to be useful to neurophysiologists for the following reasons:

(1) Its simplicity: the classical routine histological methods can be used without modification.

(2) The marks can be easily found, and, because of the presence of the halo around the central point, are not liable to be confused with artefacts.

(3) Its reliability: whereas many methods give very irregular results, we have found that with this method the number of failures is very small.

We hope that an extensive use of this method will confirm these results.

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Mechanisms of Nerve Impulse Initiation in a Pressure Receptor (Lorenzinian Ampulla)

Elasmobranchs have a well-developed system of large tubular sense organs, the Lorenzinian ampullæ[1–4]. In the dogfish, each ampulla consists of a bulb-like swelling, about 0·7 mm. in diameter, located deeply in the head of the fish, and a jelly-filled tube, several mm. long, that opens in a skin pore (see inset of Fig. 1). The ampulla is innervated by a bundle of 4–8 nerve fibres that end inside the swelling. Since the findings of Sand[5] and Hensel[6] that the stationary frequency of impulses discharged by the Lorenzinian ampulla has a high temperature coefficient (Q_{10} = 2–3), the organ has been generally regarded as a thermo-receptor. But at that time, it was not yet known that not only thermo-receptors but also mechano-receptors may have such a high temperature coefficient without losing their mechano-receptor specificness[7,8]. The general morphology of the Lorenzinian ampulla suggests a mechano- rather

than a thermo-receptor function. In any event, its deep location in the head, and the relatively low thermal conductivity of the jelly of its tube, argue strongly against its being a thermo-receptor. In fact, Murray[9] has recently shown in *in situ* experiments that probing of the ampulla pore with a bristle causes a brief change in the frequency of the nerve impulses discharged. In this communication evidence will be given that the ampulla is sensitive to pressure; it produces generator potentials which increase with the internal pressure of the ampulla.

Single isolated ampullæ of the dogfish (*Mustellus canis*) were set up in a pressure chamber (Fig. 1). The tubule was cannulated and connected to a pump. Thus, the internal and/or external pressure of the ampulla could be varied over a wide range. Single axons were dissected up to the point of axon emergence from the ampulla, and the electrical activity led off that point. Under these conditions generator and action potentials of the order of 0·1 mV. are recordable.

When the internal pressure of the ampulla is raised above its external pressure, generator potentials are produced. The amplitude of the generator potential increases with the pressure differential. The relation between pressure and generator potential is best seen when the site of nerve impulse initiation is blocked by an anæsthetic[10]. This prevents the generator current from being short-circuited at that site, and the generator potential is found to increase over a wide range of pressure (Fig. 2).

In the non-anæsthetized preparation the effect of an increment in generator current is to increase the frequency of nerve impulses. At normal atmospheric pressure on either side of the ampulla, relatively few units produce generator potential sufficiently large to set up nerve impulses. But as the internal pressure is raised, the generator potential is driven to the critical firing-level, and impulses are discharged rhythmically and continuously. When the internal pressure is raised abruptly to a new level, the discharge has a dynamic and a static non-adaptive phase. The frequency of both phases increases as a function of the pressure differential (Fig. 2).

The structures that convert pressure into generator potentials are located inside the ampulla swelling. The ampulla tube and most of the tissue of the ampulla swelling can be removed by micro-dissection[11]

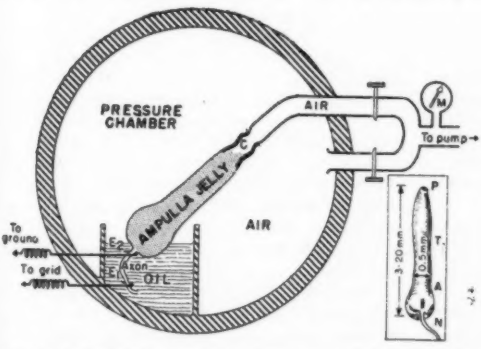

Fig. 1. The Lorenzinian ampulla is drawn over a metal cannula (*c*). Its internal and/or external pressures are varied and the corresponding generator and action potentials are led off a single axon with electrodes E_1 and E_2. Inset, some anatomical characteristics of an ampulla. *P*, Pore; *T*, tubule; *A*, ampulla swelling which contains the receptor endings; *N*, bundle of 4–8 nerve fibres

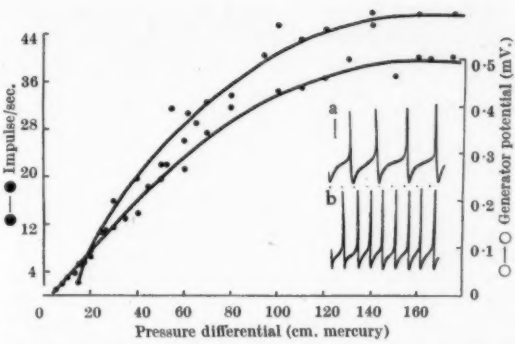

Fig. 2. Generator potential and impulse frequency as a function of pressure. The internal pressure of the ampulla is varied at constant external pressure of 1 atmosphere, and the pressure differential (abscissæ) is plotted against the amplitude of the resulting generator potential and impulse frequency (static phase). Generator potential and impulse frequency were determined in successive runs. In order to obtain a complete pressure–generator potential curve, uncomplicated by action potentials, the latter were abolished with procaine (0·08 per cent). Inset, response patterns of generator and action potentials at *a*, 40 cm. and *b*, 95 cm. pressure differential. Calibration, 50 μV.; 25 msec.

without impairment of the convertor process. The generator potential originates in, or in the immediate neighbourhood of, the nerve terminals, at a site more peripherally located than that at which the nerve impulse is started. This situation resembles that of other mechano-receptors[11–14]. The generator structures are excited effectively by an increase in the internal ampulla pressure that involves stretching, but not by increasing equally and simultaneously the internal and external pressures. A change in temperature causes an increase in the rate of rise of the mechanically elicited generator potential and thereby causes an increase in impulse frequency. But a temperature change, *per se*, produces no excitation: if the internal ampulla pressure is low so that no detectable generator potential is produced, a change in temperature, however steep its gradients, elicits no electrical response.

The Lorenzinian ampulla may thus possibly serve as a receptor of hydrodynamic pressure. In the dynamic phase of impulse discharge, the sensitivity of the receptor at about 10 metres of water (the normal cruising range of the fish) is from 5 to 12 impulses/second per metre of water pressure.

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Elevated Serum Insulin associated with Leucine-induced Hypoglycæmia

Since the original description of leucine-induced hypoglycæmia in 1956[1], much interest has been aroused concerning the mechanism by which the administration or ingestion of L-leucine or leucine-containing proteins produces a profound lowering of blood sugar-levels in susceptible individuals. Our previous experiences with two leucine-sensitive children have been reported in detail elsewhere[2,3]; the present communication deals with new and pertinent observations.

Payne and Woolf[4] reported a high blood-level of insulin-like activity following administration of leucine when compared to a fasting-level obtained a few days previously. Drs. Renold and Steinke of Boston and Drs. Yalow and Berson of New York have kindly determined for us the levels of insulin-like activity using the epididymal fat pad method[5] and the level of circulating insulin by an immunochemical technique[6], respectively.

In these experiments the L-leucine was injected intravenously[2] at a dose of 75 mgm./kgm. Zero time on Figs. 1 and 2 represents the end of a 2-hr. fasting period at which time the leucine was given. Blood samples were drawn serially during the subsequent hour. Sugar-levels were obtained for capillary blood using the method of Nelson-Somogyi[7]. Sera from venous blood were used for the determination of insulin and insulin-like activity-levels.

In Fig. 1 is shown the levels of insulin-like activity obtained by the method of Renold. The stippled bar along the ordinate indicates the limits of the values obtained in Renold's laboratory in ten normal infants less than two years of age. The maximum level was 1,450 micro-units and the mean level was 513 micro-units per ml. of serum. The solid black circles represent the results obtained on a control patient. There was no effect on the blood sugar-level (92 mgm.–86 mgm. per cent) or on the insulin-like activity. The

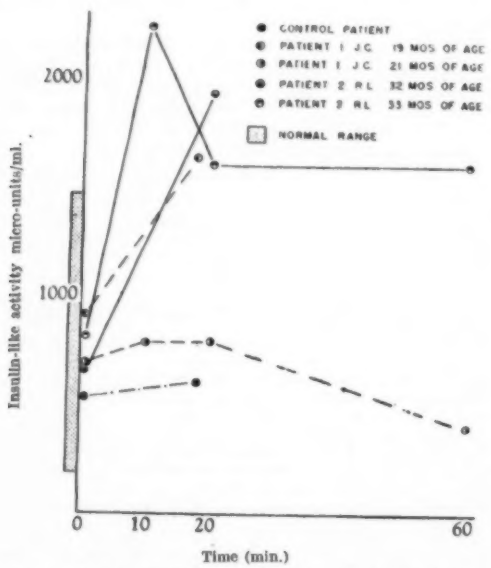

Fig. 1. Blood insulin-like activity following L-leucine administration. Method of Winegrad and Renold (ref. 5)

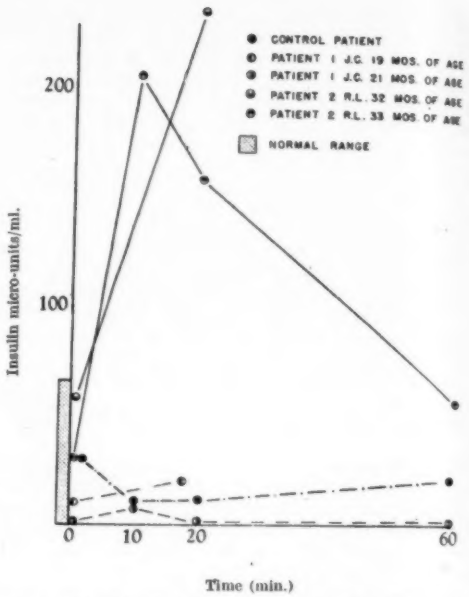

Fig. 2. Blood insulin-levels following L-leucine administration. Method of Yalow and Berson (ref. 6)

interrupted lines depict results obtained on two occasions on patient 1 (J. C.). At 19 months of age there was an increase in insulin-like activity to a level slightly above the normal range and the blood sugar-level was decreased from 84 mgm. to 38 mgm. per cent. When the test was repeated two months later, the insulin-like activity was unaltered during the course of the experiment although we observed a decline in the blood sugar-level. The solid lines depict our experiences in patient 2 (R. L.). The first test, at 32 months of age, demonstrated a significant increase in circulating insulin-like activity and the blood sugar-level decreased from 38 mgm. to 6 mgm. per cent. One month later, a second test again demonstrated a marked increase in insulin-like activity concomitant with a fall in the blood sugar-level.

In Fig. 2 are shown levels of insulin obtained by Yalow and Berson on aliquots from the same specimens from which the data on Fig. 1 were obtained. The stippled bar along the ordinate indicates the normal insulin-levels obtained by the immunochemical technique which range from virtually zero to 66 micro-units per ml. of serum. A control patient is again represented by solid circles. There was no change in either blood sugar-levels or in the circulating insulin-level during the 1-hr. test period. Patient 1 (J. C.) showed no significant changes in insulin-levels on two occasions. Patient 2 (R. L.) demonstrated very dramatic increases in circulating insulin-levels on each occasion.

Thus, we have demonstrated a significant increase of both insulin and insulin-like activity on duplicate samples of serum on two occasions in one patient with leucine-induced hypoglycæmia following the intravenous administration of leucine. In each instance there was an appropriate decrease in the blood sugar-level. In the other patient, there was no demonstrable change in the insulin-level on either of

two occasions, and the insulin-like activity was increased on only one of the two times measured.

Although we have demonstrated marked leucine sensitivity of each patient on repeated occasions, we are unable to explain the difference between these two patients with respect to the response of circulating insulin and of insulin-like activity to the administration of leucine. Other investigators have obtained data showing an increase in circulating insulin-levels in three other children with leucine-induced hypoglycæmia after the administration of leucine. These results have been communicated to us by Yalow and Berson, in whose laboratory the analyses of insulin-levels were performed. A rise of "insulin or insulin-type activity" after the administration of leucine has been reported in yet another child[8].

It would appear that in the majority of children sensitive to leucine the blood-sugar depressant activity of this amino-acid is mediated via increased synthesis and/or release of insulin. The exact mechanism by which leucine increases the circulating insulin-level is unknown. It is remarkable that in one of our two patients, hypoglycæmia followed the administration of leucine without an associated significant increase in insulin-level. The discrepancy may be explained by the presence of circulating insulin in a 'bound' form not readily detectable by the techniques employed. Other possible explanations also are now being tested.

This investigation was supported in part by research grants from the National Institutes of Arthritis and Metabolic Diseases (*A*–3581 (*A*)) and Mental Health (*M*–2673), U.S. Public Health Service.

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ANATOMY

X-ray Diffraction Study of Acellular Teleost Bone

THE osseous endoskeletons of the higher orders of teleost fish are noteworthy in that they are totally devoid of enclosed osteocytes (Fig. 1)[1,2]. The osseous tissue of other fish, like that of all other vertebrates, contains enclosed osteocytes. Although acellular bone, *per se*, is phylogenetically a very ancient tissue[3], its appearance as the sole osseous element in the skeletal systems of the most highly evolved and successful fish suggests that possession of such a tissue confers an adaptive value to the organism in a marine environment.

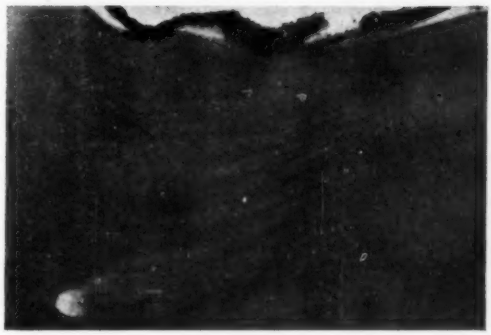

Fig. 1. Operculum of the zebra fish (*Pterois volitans*), a typical acellular bone form. Note the absence of enclosed osteocytes. (× 450)

A taxonomic classification of the distribution of these two bone tissue types in fish is under way. Preliminary observations by Moss[4] indicate that the classification of Kölliker[1] and of Berg[5] require further study.

The histogenesis of acellular bone is also unusual. The osteoblastic cells become incorporated within a matrix of their own production. There is an almost immediate cellular necrosis following which the cell spaces totally disappear, becoming filled with a substance indistinguishable from that of the surrounding calcified matrix. A more complete description of the osteogenic and reparative processes of this tissue will be published elsewhere.

An X-ray diffraction study was undertaken to seek further information on the structure of piscine bone. Two fish were used, Spanish mackerel (*Scomberomorus maculatus*) which has acellular bone, and the carp (*Cyprinus carpio*) which has cellular bone tissue. The skulls of several adults of each species, freshly caught, were soaked in water, scraped and cleaned. The separate samples were pulverized in a Waring blender and dried over calcium chloride. The material was then ground by hand in a mullite mortar for X-ray diffraction examination.

The X-ray diffraction powder patterns (Fig. 2) were taken on a 'Norelco' diffractometer using nickel-filtered copper *K*-radiation, with a 1-deg. slit system, and an argon-filled Geiger–Müller counter as a

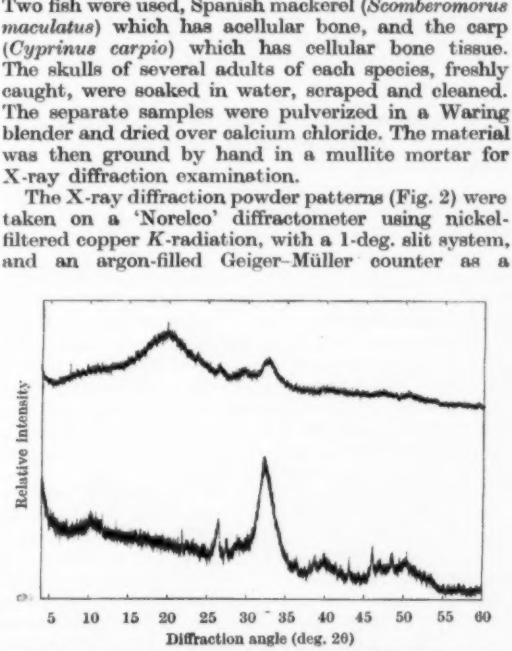

Fig. 2. Comparison of X-ray diffraction powder patterns of acellular (Spanish mackerel) fish bone (upper) and cellular (carp) fish bone. Nickel-filtered copper *K*-radiation was employed. The broad peak on upper pattern at about 20° 2θ is probably due to a large collagen component in the acellular bone

detector. The latter was set to travel through the goniometer arc at a speed of $\frac{1}{4}°$ 2θ per min.

Fig. 2 shows typical X-ray diffraction patterns of the two specimens. Both patterns indicate the presence of a finely divided hydroxyapatite phase. The apatite crystals in the acellular bone (upper curve) appear to be smaller and/or more strained than the cellular bone crystals (lower curve) as evidenced by the broader X-ray diffraction maxima due to apatite seen at about 26° 2θ, 29° 2θ, and 32° 2θ. There is a much larger organic fraction, probably collagen, in the acellular bone than in the cellular bone. This is shown by the prominent, broad peak at about 20° 2θ which appears in the acellular pattern but not in the cellular X-ray diffraction pattern.

The role of acellular bone in the mineral homeostasis of the fish and the structure of such bone is being further investigated[6].

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A Microscopic Method of determining Rates of Bone Growth

The measurement of accretion-rates of bone by a non-toxic, non-radioactive, direct method based on the intravital marking of growing surfaces would be of value[1]. I have been studying intravital staining of growing-bone surfaces in man, dogs, and rats, using many agents including alizarin red *S*, chlorazol fast pink[2], chlorazol sky blue, calcium fast purple, naphthamine brilliant blue *RR* and the tetracyclines. My aim was to be able to define microscopically the amount of growth in a stated time interval. By far the most satisfactory are the tetracyclines. Chlortetracycline, oxytetracycline and tetracycline are selectively incorporated into new bone deposits and can be identified by their fluorescence. They remain detectable for at least six months[3].

Fig. 1 shows the growth of two canine osteons over a twelve-week period. The outer ring in each system is a deposition of alizarin red *S*, which is less suitable for this work than tetracyclines because of its systemic toxicity. Next is a chlortetracycline ring (33 mgm./kgm. intravenously given four weeks later). The next ring is a marker of oxytetracycline (62·5 mgm./kgm. intravenously, 8 weeks after the alizarin). The last line is made by 33 mgm./kgm. intravenously of chlortetracycline 12 weeks after the alizarin and 72 hr. prior to killing the animal. The

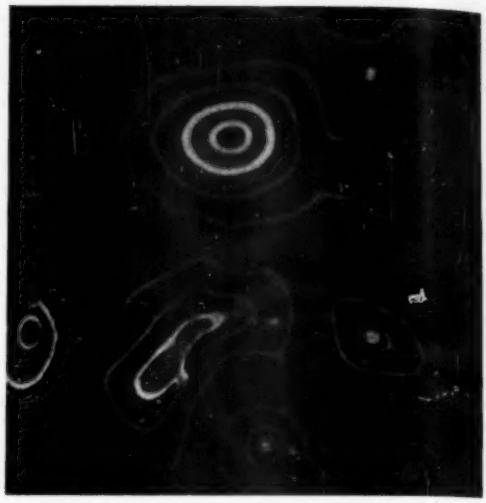

Fig. 1

upper system in the illustration demonstrates growth varying from 28 to 60 microns during the first four-week period, from 28 to 52 microns during the second, and from 26 to 48 microns during the third.

The width of the line of initial uptake may be wider than the subsequent width of that line (compare the second and fourth lines, which both result from a dose of 33 mgm./kgm.). The relationship of this to changes occurring in the osteoid and at the calcification front is not yet known.

Ghosez[4] and Ponlot[5] have shown that the microscopic localization of tetracycline uptake is strongest at the peripheral portion of the pre-osseous layer, that is, the calcification front and region just preceding it.

The submicroscopic specific site of tetracycline uptake is unknown. However, so long as measurements are made between two tetracycline lines, this information is not required for measurements of the area of new bone deposit.

62·5–80 mgm. of tetracycline intravenously produce less-suitable lines because of their width and the flare that accompanies more intense deposits. Moreover, these doses may produce a partial inhibition of mineralization (unpublished work). Chlortetracycline, but not oxytetracycline or tetracycline, can occasionally produce a minimal decrease in mineralization of canine bone at doses as low as 33 mgm./kgm. intravenously. Therefore, 20 mgm./kgm. intravenously of oxytetracycline is recommended for work with dogs. In recent experiments with rats, demethylchlortetracycline showed greater intensity of fluorescence than identical doses of the other three. This may be related to its sustained blood-levels. A satisfactory mark is given in human bone by two oral doses of 1 gm. of any of the tetracyclines, 6 hr. apart.

Undecalcified sections must be used, since the tetracyclines are removed by acid or ethylenediamine tetraacetate. The width of the marker in thin transverse sections (less than 40μ thick) is less than 8μ for tetracycline doses of 33 mgm./kgm. intravenously, provided that the growing surface was reason-

ably perpendicular to the plane of section. This resolution exceeds that of calcium-45 (ref. 6) and radium (ref. 7), but not the optimum possible with plutonium-239 (ref. 8). The resolution and non-toxicity make this method preferable to lead[9].

A high-pressure mercury vapour lamp, collecting lens and Wratten 18*A* filter provide a good source of ultra-violet light. Most ordinary bright-field microscopic equipment is satisfactory for this type of ultra-violet work. A Wratten 23*A* filter in the eyepiece reduces transmission of the blue auto-fluorescence of non-labelled bone and permits satisfactory black-and-white photography. More details on the ultra-violet microscopy are given in a paper by Kuper and May[10].

Chlortetracycline, tetracycline and demethylchlortetracycline were supplied by Lederle Laboratories Division of Cyanamid of Great Britain, Ltd., under the trade names 'Aureomycin', 'Achromycin' and 'Ledermycin', respectively. Oxytetracycline was supplied by Pfizer, Ltd., under the trade name 'Terramycin'.

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PATHOLOGY

Cytochemistry of Nucleic Acids in Murine Lymphoma Cells infected with Polyoma Virus *in vitro*

Infection of cultures of milk-adapted $P388D_1$ murine lymphoma cells with polyoma virus produces an alteration in the ribonucleoprotein (RNP) of the nucleoplasm, enlargement of the nucleolus, and intranuclear vacuoles containing abnormal RNP[1]. Cytochemical studies of the late stages of infection of lymphoma cells *in vitro* with polyoma virus failed to reveal Feulgen-positive inclusion material[1]. Since the infectivity of nucleic acid preparations from cells infected with polyoma virus appears to reside in the deoxyribonucleic acid (DNA) fraction[2], further attempts have been made to demonstrate abnormal DNA and to elucidate the relationship between changes in DNA and RNA or RNP metabolism in polyoma virus infection.

Three day-old cultures of milk-adapted $P388D_1$ lymphoma cells were infected with a 10^{-1} dilution of the fourteenth serial passage of polyoma virus as previously described[1]. The cells were examined at intervals of 24, 48, 52, 72 and 96 hr. after infection. Some modifications of the previous cytochemical staining procedures[1] were introduced. The intensity

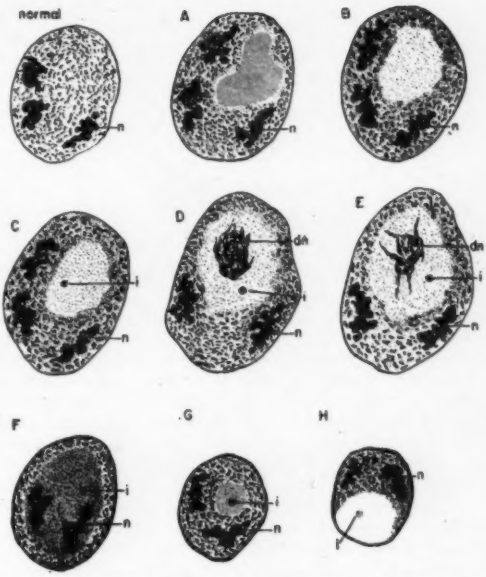

Fig. 1. Nuclei of $P388D_1$ lymphoma cells stained with toluidine blue-molybdate (stage III). *A*—*H* represent stages in the evolution of the lesions. *n*, Nucleolus; *i*, inclusion; *dn*, degenerating nucleolus

of staining was increased by a brief saline rinse before fixation. Hydrolysis of the Feulgen preparations for 30 min. gave more intense staining than the usual 10-min. hydrolysis. Cultures were also stained with acridine orange after fixation in absolute ethanol[3].

Definite lesions were recognized 48 hr. after infection. The pathogenesis was assessed mainly from the time sequence of the changes, but in part by analysis of the increasing disorganization of nuclear structure (Fig. 1). Enlargement of the nucleus and nucleolus was the earliest change and this was accompanied by the appearance of homogeneous intranuclear zones or vacuoles filled with Feulgen-positive DNA (Figs. 1*A* and 2). These Feulgen-positive areas were also stained by toluidine blue-molybdate (TBM), stage III (ref. 4), after ribonuclease digestion. Later, an increasing number of cells with unstained vacuoles or ill-defined clear zones were noted (Figs. 1*B* and 2). Small round homogeneous inclusions then appeared in the vacuoles (Fig. 1*C*). The inclusions stained less strongly than the chromatin but were definitely

Fig. 2. One normal (top left) and two infected $P388D_1$ lymphoma cells, one of which (left) has an intranuclear vacuole filled with DNA, cf. Fig. 1, normal, *A* and *B*. Feulgen stain. (× 1,400)

Fig. 3. Intranuclear inclusion body. Feulgen stain. (× 1,400)

Feulgen-positive (Fig. 3). Since the intensity of staining of the inclusions by TBM (stage III) was unaffected by ribonuclease digestion they did not contain any detectable RNA at this stage. Afterwards one or more of the enlarged nucleoli stained less intensely and became more diffuse (Fig. 1*D*). This nucleolar material formed one or more ill-defined masses (Fig. 1*E*) and eventually filled the clear spaces or vacuoles (Fig. 1*F*). The intensity of staining of the inclusions by the Feulgen procedure decreased during this period and the inclusions were more strongly coloured by TBM (stage III). Staining by TBM (stage III) was greatly reduced, but not abolished, by pre-treatment with ribonuclease, indicating that the inclusions contained RNA as well as DNA. Further nuclear disorganization was caused by shrinkage (Fig. 1*G*) and in many shrunken cells RNP could no longer be detected in the vacuoles (Fig. 1*H*). At this stage the inclusions were stained dark green by TBM (stage III) with or without previous ribonuclease digestion and were clearly Feulgen-negative (compare ref. 1, Fig. 9). The inclusions, therefore, no longer contained the nucleolar type of RNP which stains purple in stage III TBM preparations[4]. After very brief fixation (2 min.) in formol sublimate at 37° C., the inclusions stained intensely purple with TBM. In such preparations the inclusions were stained dark green after ribonuclease digestion and not at all after ribonuclease and crystallized deoxyribonuclease (Mann Labs. Inc.) digestion. All staining by TBM was prevented by extraction of nucleic acids with hot trichloracetic acid. The inclusions could not be distinguished from other masses of chromatin in the acridine orange or in the pyronin methyl green preparations. Protein-bound amino and other groups were demonstrated in the inclusions by the ninhydrin–Schiff procedure[1]. In the final stage of nuclear degeneration the thin circumferential wall of the vacuole ruptured and the inclusions could be seen in the adjacent cytoplasm.

The course of polyoma virus infection is interpreted as follows. The normal DNA of the chromatin breaks down to form amorphous Feulgen-positive DNA. DNA is not detectable in the next stage of infection, although it may exist as low molecular weight material which is not preserved by fixation. Inclusions containing DNA then appear and are surrounded by and incorporate RNA of nucleolar origin. As the RNA, and presumably the protein, of the inclusions increases they become less Feulgen-positive. Finally, nucleolar RNP can no longer be detected in the inclusions and they contain another form of RNA, DNA and protein. The failure to stain by the Feulgen procedure is probably caused by physical rather than chemical interference with the staining reaction by viral protein. A similar phenomenon has been observed during the formation of vaccinia virus (Love, R., and Salzman, N. P., unpublished work); the cytoplasmic inclusion is strongly Feulgen-positive in the early stages of infection and becomes less so as the viral particles are formed.

We wish to thank Frances Y. Legallais and Roscoe H. Liles for valuable technical assistance and Joyce L. Sills for the drawings.

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Leptospira pomona Infection in an Eastern Red Fox (*Vulpes fulva fulva*)

The presence of leptospirosis in Pennsylvania cattle has been well established[1–3]. An epizootiological investigation to determine the relationship between bovine and sylvan leptospirosis is at present being undertaken in south-eastern Pennsylvania. Infected cattle herds are identified and their premises intensively trapped for wild-life. Trapped animals are examined for infection by serological and cultural techniques. Isolations of leptospires have been made from the following animals: woodchuck[4], opossum, skunk, racoon and Norwegian rat. This communication is believed to be the first to report the isolation of *Leptospira pomona* from an eastern red fox (*Vulpes fulva fulva*)[5]. The fox was trapped on the premises of a known infected cattle herd. Prior to the start of trapping, *Leptospira pomona* had been isolated from cattle and from surface waters on this farm.

The fox was caught in a No. 2 coil-spring trap, removed from the trap and delivered to the Leptospirosis Laboratory, School of Veterinary Medicine, University of Pennsylvania. On delivery, the fox was euthanized in a carbon monoxide chamber. A blood specimen was obtained by severing the jugular vein and collecting the flow. One kidney was removed aseptically.

The kidney was ground with pestle and mortar and diluted to approximately a 10 per cent suspension with Stuart's base liquid medium ('Difco'). Two tubes of each of the following media were inoculated with 2–3 drops of kidney suspension: Fletcher's semi-solid medium containing 15 per cent horse serum; Chang's semi-solid medium[6] (Hamilton, Montana, modification[7]) containing 10 per cent rabbit serum; Chang's semi-solid medium containing 15 per cent horse serum; and Stuart's semi-solid medium[8] containing 10 per cent rabbit serum. Tubes were incubated at 29° C. and examined at 10–14 day intervals by dark-field microscopy.

Serum from the blood specimen was examined for antibody content by the microscopic agglutination test[9], employing an antigen bank of eleven serotypes: *L. bataviae*, *L. pomona*, *L. autumnalis*, *L. ballum*, *L. canicola*, *L. icterohemorrhagiae*, *L. alexi*, *L. grippotyphosa*, *L. australis A*, *L. sejroe* and *L. hyos*.

Growth of leptospires was detected on day 34 post-inoculation. Organisms were present in one tube of each of the following media: Fletcher's semi-solid

medium containing 10 per cent rabbit serum, Fletcher's semi-solid medium containing 15 per cent horse serum, and Chang's semi-solid medium containing 15 per cent horse serum. Transfers were made into Fletcher's semi-solid medium containing 10 per cent rabbit serum and into Stuart's liquid base medium containing 10 per cent rabbit serum. Subcultures made at 10–20 day intervals were sent to the Leptospirosis Unit, Animal Disease Eradication Diagnostic Laboratory, United States Department of Agriculture, Ames, Iowa, for typing. They were identified as *Leptospira pomona*.

The microscopic agglutination test titres were: *L. pomona*—1 : 100; *L. autumnalis*—1 : 1,600.

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BIOLOGY

Juvenile Hormone Activity in Micro-organisms and Plants

THE juvenile hormone of insects promotes larval development but prevents metamorphosis. Its presence in an immature insect ensures that when the larva molts it will retain its larval characters and not differentiate into an adult[1]. Extracts with juvenile hormone activity were first prepared from the abdomens of male *Cecropia* moths by Williams[2]. Afterwards active extracts were prepared from adult males and females of 6 families of Lepidoptera as well as from eggs, larvæ and newly moulted pupæ[3,4], from representatives of 6 other orders of insects including Dictyoptera, Orthoptera, Hemiptera, Coleoptera, Diptera and Hymenoptera[4–7] and from various insect products, for example, royal jelly[7], insect fæces[8]. Investigation of other groups uncovered substances with juvenile hormone activity in extracts of the adrenals of cattle[9] and in many tissues of numerous invertebrates in 13 classes, including Hydrozoa, Anthozoa, Anopla (Nemertinea), Cheilostomata and Ctenostomata (Ectoprocta), Polycepoda, Gastropoda, Polychaeta, Oligochaeta, Malacostraca, Arachnida, Holothuroidea and Balanoglossida[6,7]. The most active invertebrate sources were the eyestalks of crustaceans (*Homarus* and *Carcinides*)[6,7], and the heads of polychaetes (*Nereis*)[7]. Juvenile hormone activity was later demonstrated in many vertebrate tissues besides the adrenals including pituitary, kidney and thymus[10] and lymphatic, parathyroid, thyroid, mammary and gastric mucin (Schneiderman, H. A., and Gilbert, L. I., unpublished observations).

All these active extracts prevented certain tissues of young insects from assuming their adult aspect, but did not interfere with growth itself. In pupæ of Lepidoptera, Hemiptera and Coleoptera, local application of active extracts caused the pupal epidermal cells to lay down a second pupal cuticle while untreated cells nearby deposited normal adult cuticle[2,3,5,6,11].

The present communication reports the occurrence of juvenile hormone activity in extracts of several micro-organisms. Ether or chloroform extracts were prepared from whole ferments (that is, cells plus media) as well as from washed organisms. In those cases where non-synthetic media were used, the uninoculated medium itself was also extracted and tested after autoclaving. Extracts of more than 60 organisms were prepared and assayed for their juvenile hormone activity by the 'Polyphemus' wax test[4] and by other procedures[5,11]. The 'Polyphemus' wax test can detect juvenile hormone activity in extracts with 1/2,000th to 1/10,000th as much activity per gm. as oil extracted from male *Cecropia* moths, whereas the other tests are less sensitive. Extracts of 6 species of micro-organisms had juvenile hormone activity in both the 'Polyphemus' wax test and in at least one other test for juvenile hormone activity[5,11]. These included a ciliate, a flagellate, two bacteria and two yeasts. A representative sampling of the results is recorded in Table 1.

Table 1. JUVENILE HORMONE ACTIVITY OF MICRO-ORGANISMS

Name	Type of extract	Percentage of positive tests	Activity
Ochromonas malhamensis	ether	45	++
Tetrahymena pyriformis	ether	18	+
Euglena gracilis	ether	0	0
Chilomonas paramecium	ether	0	0
Baker's yeast (fresh)	ether	25	+
Brewer's yeast (dried)	ether	100	++
Saccharomyces (eight other species or strains)	chloroform	0	0
Schizosaccharomyces (2 species)	chloroform	0	0
Hansenula anomala	chloroform	0	0
Dipodascus uninucleatus	chloroform	0	0
Debaryomyces disporus	chloroform	0	0
Trichosporon pullulans	chloroform	0	0
Nadsonia elongata	chloroform	0	0
Endomycopsis fibuliger	chloroform	0	0
Lipomyces lipofer	chloroform	0	0
Micromonospora sp. (mycelium)	chloroform	65	+
Streptomyces (seven species or strains)	chloroform	0	0
Escherichia coli (washed cells)	ether	0	0
Escherichia coli (cell-free broth)	ether	75	+++
Proteus spp. (whole broth)	ether	75	+++

In the course of assaying various bacteriological media it was discovered that ether extracts of soy bean meal had juvenile hormone activity, indicating that juvenile hormone activity is not only found in lower plants but in higher plants as well.

Despite some efforts, no activity could be obtained from well-chilled diapausing pupæ or from allatectomized male adults of *Cecropia*. Nor was activity found in lipid extracts of sponges and of numerous familiar animals such as the sea anemone *Metridium dianthus*, the long-necked clam *Mya arenaria*, the horseshoe crab *Limulus polyphemus* and many others. Activity also appeared to be absent from various vegetable oils such as castor oil, wheat germ oil, palm oil, coconut oil, peanut oil, corn oil, olive oil, linseed

oil and cotton seed oil as well as from bees wax, carnauba wax, paraffin wax and ceresine wax. It was also absent from most of the micro-organisms examined. This lack of activity did not seem to be due to the presence of inhibitors in the inactive preparations, for in most cases addition of inactive extracts to active extracts did not cause a loss of activity.

These results indicate that we are dealing with a group of substances which are widespread in Nature, but are probably not universal. Indeed, one would scarcely imagine insects adapting a universal and indispensable molecule as a hormone. It is nevertheless intriguing that substances that can mimic an insect growth hormone occur in protozoa, fungi and mammals. These findings support the opinion offered earlier[8,12], that in many cases the development of humoral mechanisms involves not so much evolution of hormones as such, but more the evolution of target mechanisms which acquire a sensitivity to specific small molecules that may have been present from earliest times, and the development of systems that can ensure the timely production of appropriate amounts of these specific molecules. As Hisaw puts it, often " . . . it is not hormones which have evolved but the uses to which they are put. . . ."[13].

We wish to express our thanks to Prof. George Holz of Syracuse University, who provided us with Protozoa for extraction.

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A Possible Function of Phycoerythrin in Intertidal Red Algae

The transmission of light in coastal waters is such that penetration is greatest in the blue-green and least in the red region of the visible spectrum[1]. This has led to the view that the phycobilins, accessory pigments that give rise to the characteristic colour of red algae, are responsible for photosynthesis by these plants because, unlike chlorophyll, the pigments readily absorb blue-green light[2]. Evidence in favour of this theory of complementary chromatic adaptation has been obtained by Haxo and Blinks from experiments in which the action spectra of several marine red algae were found to show a fair correlation with the absorption curves of phycoerythrin and phycocyanin[3].

Continuing recent work on the factors affecting the ecological distribution of certain red algae[4], we have become interested in the way light influences the growth of sporelings of these plants, and have made some preliminary experiments using *Plumaria elegans* (Bonnem.) Schm., a shade-loving species which inhabits the lower mid-littoral zone. We have extracted the red pigment from this plant and find that it has an absorption curve characteristic of phycoerythrin (peaks at 500 and 550 mμ). It is, therefore, well able to absorb blue-green light, and if the theory of complementary chromatic adaptation holds in the case of *Plumaria* sporelings, they would use this light for photosynthesis. To test this we grew sporelings in filtered sea water enriched with Erd-Schreiber medium[5], contained in glass vessels screened from the light source by weak solutions of phycoerythrin, prepared freshly each day. We measured the rate of growth of the plants by counting the number of cells produced by a crop of approximately 200 sporelings during a ten-day period, the method used being one already described[6]. Contrary to expectation, sporelings screened in this way grew at more than twice the rate of the control material.

Because of the instability of solutions of phycoerythrin, we carried out subsequent experiments using a screen 2 cm. thick of a weak sea water solution (0·2 p.p.m.) of the dye eosin yellow, which also has an absorption peak in the blue-green region (515 mμ). Over the very wide range of light intensities used, including some below and some above optimum value (315 lux), it was found that the screened sporelings had a much more marked rate of growth (see Fig. 1).

At first it seemed possible that the dye was protecting the sporelings by removing ultra-violet light inhibitory to their growth. However, this possibility can be excluded because the distribution of spectral energy of the source used, an 'Ekco Daylight' fluores-

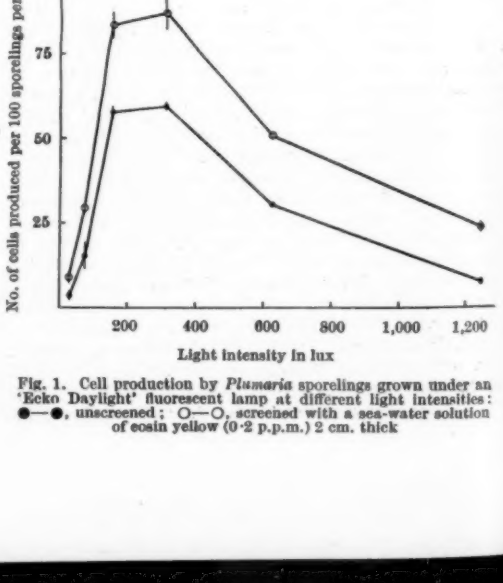

Fig. 1. Cell production by *Plumaria* sporelings grown under an 'Ekco Daylight' fluorescent lamp at different light intensities: ●—●, unscreened; ○—○, screened with a sea-water solution of eosin yellow (0·2 p.p.m.) 2 cm. thick

cent lamp, showed very little energy in the ultra-violet region, and even this small quantity was further reduced by the glass vessels used in the experiment. Moreover, the very weak screening solution of eosin yellow had no measurable effect on the small amount that remained.

The possibility that the dye solution was enhancing growth simply by shading the sporelings is also excluded. For at sub-optimal light intensities, shading would obviously inhibit growth, whereas it was found that the screened sporelings grew faster at a light intensity as low as 30 lux. Furthermore, even at the highest light intensity used (1,250 lux) shading would influence growth to an insignificant extent because the very weak solutions of the dye only absorbed 2·2 per cent of the total light energy in the wave-band 390–700 mμ, and it can be estimated from Fig. 1 that more than 15 times this amount would have to be removed to account for the difference in growth between screened and control sporelings.

It therefore appears that both eosin yellow and phycoerythrin, as used under our experimental conditions, promoted the growth of the sporelings by protecting them from the inhibitory effects of blue-green light emitted by the fluorescent tube, a light source with a spectral energy distribution closely resembling that of daylight. Accordingly, it seems that the theory of complementary chromatic adaptation does not apply in the case of *Plumaria*.

It is hoped to publish a fuller account of this work in the *Journal of the Marine Biological Association*.

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Growth Movements of the Radicle of *Striga*

The directional growth of the radical (haustorium) of the root parasite *Striga asiatica* (= *S. lutea*) is normally controlled by a chemotropic factor diffusing from the host plant root[1]. The parasite seeds may be germinated by treatment with a solution in which the host roots (*Sorghum vulgare*, etc.) have been growing. In this case the radicle undergoes a fixed growth movement which is roughly spiral. A basically spiral movement is seen in about 40 per cent of seedlings. More usually the movement is reduced to a strong curvature in one plane followed by a period of more or less straight growth, or by apparently anomalous curvatures in any direction. By growing the seedlings in agar cultures, it was shown that the movements were not influenced by the orientation of the seedlings to gravity or by rotation on a klinostat, at least during the initial curvature, although with

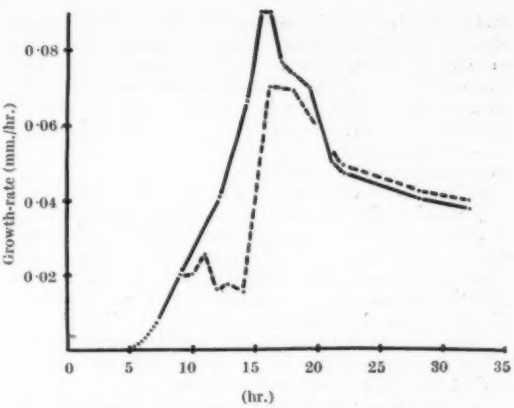

Fig. 1. Average growth-rates (11 seedlings) of the fast-growing (——·) and slow-growing (– – –·) sides of the *Striga* radicle during curvature and subsequent straight growth

forces greater than gravity (up to 10*g*) a positive movement was superimposed on the fixed growth movement.

The initial curvature in one plane was used in studying quantitative aspects of the movement. For this purpose seedlings were grown in Petri dishes, growth and curvature being recorded throughout development using a camera lucida in combination with a low-power microscope. The culture dishes were housed on the microscope stage in a light-proof box fitted with removable flaps to permit observation.

An analysis of curvature revealed that this was always associated with an inhibition of cell extension on one side of the radicle, which gave rise to a divergence from a normal sigmoid pattern of growth which characterized the growth of the opposite side (Figs. 1 and 2*A*). The initial period, during which the growth-rates of the two sides was equal, represents a phase of general swelling of the embryo and the commencement of meristematic activity.

In attempting to determine the nature of the factor causing this inhibition, the effects of various anti-auxins on growth and curvature were tested. The anti-auxin 2 : 3 : 5-tri-iodobenzoic acid had a striking effect in reducing curvature, by eliminating the differential inhibition of cell growth on the inner side of the curve (Fig. 2). At a level of 1 p.p.m., 2 : 3 : 5-tri-iodobenzoic acid strongly reduced curvature while

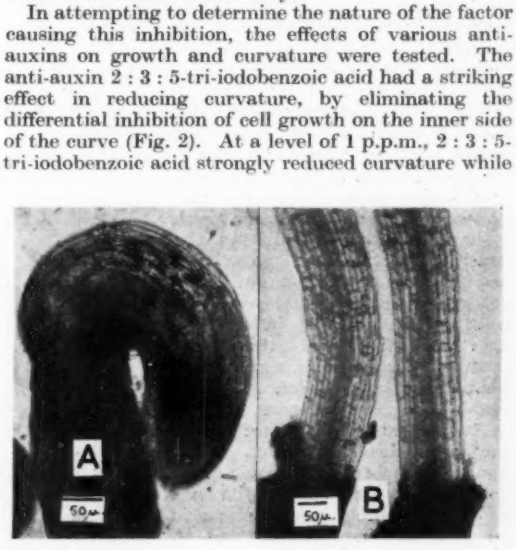

Fig. 2. *A*, *Striga* seedling showing initial curvature of the radicle; *B*, effect of 2 : 3 : 5-tri-iodobenzoic acid (1 p.p.m.) on curvature

linear growth was only reduced by about 20 per cent. Jones *et al.*[3] record that 2 : 3 : 5-tri-iodobenzoic acid reduced geotropic response in rape and rye-grass, but this only occurred at a level which was markedly inhibitory to linear growth. At higher concentrations of auxin; the anti-auxins 2 : 4 : 6-trichlorophenoxyacetic acid showed lateral expansion of cells and considerable reduction of linear growth.

Although the effect of 2 : 3 : 5-tri-iodobenzoic acid suggests that the curvature factor may be some form of auxin, the anti-auxins 2 : 4 : 6-trichlorophenoxyacetic acid and 2 : 4-dichloroanisole, which are supposed to act competitively with auxin at the growth centres, did not selectively reduce curvature. This indicates that the curvature factor, if some form of auxin, must be protected from the competitive action of these anti-auxins. One possible explanation is that the factor may be transferred selectively from a bound form (which could be some auxin/protein association) to the receptive centres for the growth reaction, or that certain places in the growth system are reserved for the curvature factor. The comparative immobility of the curvature factor (that is, not being ordinarily influenced by gravity or rotation on a klinostat) would indicate an association with structural or immobile constituents of the cell. 2 : 3 : 5-tri-iodobenzoic acid, on the other hand, could act at some site before the growth centres, which would be in agreement with Lineweaver–Burk data on the action of 2 : 3 : 5-tri-iodobenzoic acid.

Growth curvatures in other roots are known to be associated with a marked inhibition of extension growth[2,4], and various considerations have led to the view that curvature does not result from a redistribution of polar auxin, but from the production of a specific growth inhibitor on one side of the root. Audus and Brownbridge[3] tested the effect of indoleacetic acid on the geotropic curvature of pea roots (which are stimulated by low concentrations of auxin) and found that both the lower and upper sides of the roots were stimulated to grow faster by low concentrations of indoleacetic acid (that is, the inhibited lower side, in which the auxin-level would presumably be supra-optimal if this substance is the curvature hormone, was also stimulated). This indicates that the curvature hormone in pea roots is not indoleacetic acid, or differs in some way from externally applied indoleacetic acid. The action of the anti-auxin α-(1-naphthyl-methylsulphide) propionic acid in reducing curvature in these roots (Audus and Brownbridge[5]) is attributed to the action of this substance on some endogenous inhibitor which is not indoleacetic acid, and the general promotion of growth of pea roots by this anti-auxin, to its action on residual inhibitors in the cells. The fact that indoleacetic acid and this anti-auxin show mutual antagonism[6] is now explained by competition at a site outside the growth centre.

Audus and Thresh[7], using paper partition chromatography, found that 2 : 3 : 5-tri-iodobenzoic acid reduced in a striking way the level of alcohol-soluble indoleacetic acid in pea seedling tissues, and at the same time induced a negative geotropic response in the side roots of the seedlings; although the possibility that this substance may not actually be indoleacetic acid is indicated by the work of Bennet-Clark *et al.*[4] on the isolation of plant growth substances using starch column chromatography. This shows that a substance distinct from, but appearing like, indoleacetic acid in paper partition chromatography is present in root tissues.

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Variations in Scopoletin in Leaves in Relation to Chloride Treatment of Tobacco

High concentrations of sodium chloride in the soil have an adverse effect on the growth of the tobacco plant. Stunted plants, with thickened leaves containing large quantities of starch, have been reported, and the leaf colour also is affected[1]. Thickening of the secondary xylem elements[2] is also attributed to the effect of high chloride concentrations.

Scopoletin, as well as being a normal constituent of tobacco leaves, has been found to increase markedly in the case of attack by the tomato spotted wilt virus[3] and to be present in higher concentration in differentiating than in non-differentiating tobacco tissue[4]. Scopoletin also acts as an inhibitor of the enzymic destruction of indoleacetic acid and could thus itself act as a growth inhibitor by causing indoleacetic acid to accumulate beyond the stimulatory range[5].

Using fluorescence under ultra-violet light, paper chromatographic studies[6,7] of aqueous and methanolic extracts of oven-dried green tobacco leaves from plants, variety Hicks, grown in sand in the glass-

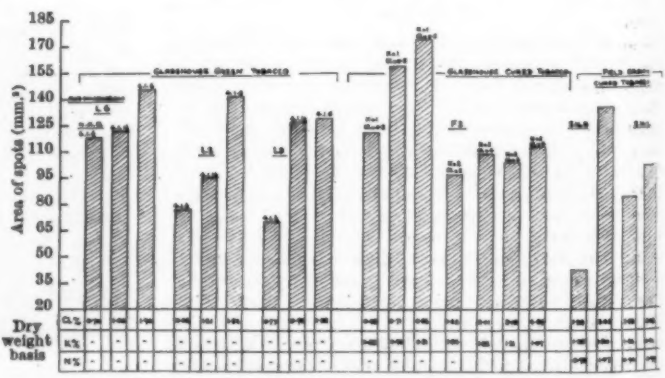

Fig. 1. Scopoletin in tobacco leaves in relation to chloride

house with concentrations of sodium chloride ranging from 0·5 to 6·0 milli-equivalents per litre in the applied nutrient solution, have shown that increased chloride in leaves of the same physiological age is associated with increased scopoletin (Fig. 1). Glasshouse-cured tobacco leaves and field-grown cured leaf also show similar relationships in scopoletin and chloride content, and calculations based on the assumption that the spot area is proportional to the logarithm of spot content[6] give concentrations of scopoletin varying approximately from less than two to one hundred and seventy times greater in the leaf with high-chloride than in one containing a low-chloride concentration.

The increase in scopoletin associated with a higher chloride content in the leaf may account for the typical morphological and anatomical effects produced both in the leaf and generally in the plant: the stunting (also noticeable in virus attack[3]) being due to the effect on the indoleacetic acid metabolism, and the thickening of the secondary xylem to increased concentrations of scopoletin at the site of the differentiating tissue. Scopoletin concentrations in the root and stem of tobacco plants under varying chloride treatments are being examined.

As scopoletin passes unchanged into the mainstream smoke on combustion of the tobacco[6], it may be an important factor in tobacco quality as influenced by sodium chloride in the soil. Other factors which affect the nutrient balance, such as low potash content, also appear to favour the accumulation of scopoletin.

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Function of the Osphradium in *Bullia* (Gastropoda)

Krijgsman and Brown[1] have recently described a technique for operating on fully extended and immobilized marine Gastropoda. We have now used this 'water-rigour' method on 124 individuals of *Bullia laevissima* (Gmelin) preparatory to severing their osphradial nerves in order to discover the function of the osphradium. The osphradium in Gastropoda is generally thought to be an organ of chemo-reception, though the evidence in support of this theory is far from satisfactory. Experiments such as those of Copeland[2] are not convincing in view of the crude techniques used. A few workers, notably Hulbert and Yonge[3], have suggested that the osphradium may be concerned with the perception of turbidity; but no experimental data have been presented in support of this view, the only evidence being circumstantial. Detailed histological studies of the osphradium, such as those undertaken by Stork[4], add little to the argument.

Of the 124 snails on which we operated, 52 did not recover and post-mortem examination revealed damage to the pallium and/or the dorsal pallial artery which passes just below the osphradium. When the remaining 72 snails were killed and dissected after the completion of our experiments, it was found that in some cases the osphradial nerve had not been completely severed, while in others nerves other than the osphradial nerve had been cut or damaged accidentally. The results of experiments on these snails were therefore disregarded. In only 13 cases was the operation completely successful, the osphradial nerve being entirely severed without damage to other structures. Of these 13 snails, 12 lived for more than a week in the laboratory and were offered food on each successive day.

Bullia laevissima normally lies half buried in the sand, under water, only the upper part of the shell and the siphon being visible. It can be caused to emerge actively from the sand if suitable food be placed in or near the water. (A detailed account of this behaviour is given elsewhere by Brown[5].) However, individuals which have had the osphradial nerve severed fail to emerge, even when presented with their favourite food—the tunicate *Pyura*. Nevertheless such individuals will feed when placed on the food or touching it, indicating that failure to emerge is not resultant on a disinclination to feed, but rather indicates a deficiency in chemo-perception from a distance. We are therefore of the opinion that chemo-reception is at least the major function of the osphradium in this species.

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CYTOLOGY

Number of Chromosomes in the Human Cell

Current work with human chromosomes in many laboratories has resulted in the publication of numerous photographs of chromosomes of human cells both normal and abnormal. Almost all these have been obtained from cells which are selected at least to the extent that they are cells capable of undergoing mitosis one or more times *in vitro*. These cells are often subjected to physical conditions which might conceivably influence the process of mitosis, that is, temporary chilling, change of *p*H, etc. Further, in most cases the mitotic process has been disturbed intentionally by the use of colchicine.

Because of the possible significance of these factors, we feel that the accompanying photograph (Fig. 1) will be of interest. It shows an unstained, uncolchicinized bone marrow mitosis obtained within minutes after aspiration from a 59-year-old female. There is clear representation of 46 chromosomes. The correspondence of this and other morphological details with those obtained using colchicine and tissue culture methods is to be noted. We feel this is

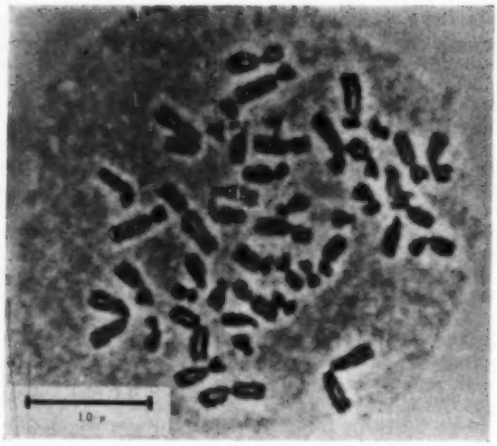

Fig. 1

important in that it demonstrates a lack of dependence of these characteristics on the use of tissue culture and colchicine.

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Growth of the Gametes of *Amoeba spumosa* Grüber

IN a previous paper[1] the biological cycle of *Amoeba spumosa* Grüber, the amoeba most often found in fresh water in Lombardy, was described and the cytological aspects of the gametes of this amoeba were studied by means of the electron microscope.

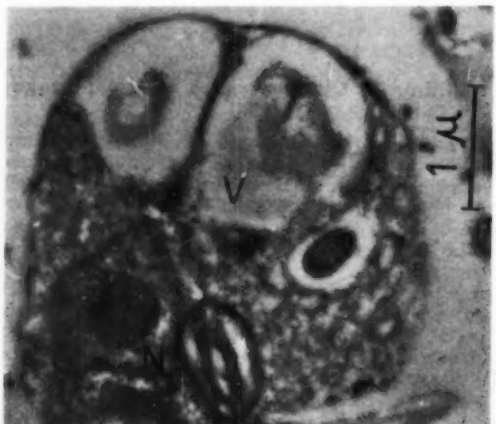

Fig. 1. Electron microscopical picture of a section of an *Amoeba spumosa* gamete. *F*, flagellum; *G*, Golgi apparatus; *N*, nucleus; *V*, vacuoles at the top end

These gametes (Fig. 1) are spherical cells, which move around by means of a flagellum, like those of *Amoeba proteus*: this observation confirms the forgotten observation of Jones[2]. The flagellum has a structure common to the flagella of other organisms: that is, it contains nine peripheral filaments and two central filaments.

The present work was carried out to study these gametes statistically, in order to ascertain their developmental biology.

Amoebæ in gametogenesis, cultured under daylight (at 19° C.), release (Fig. 2) their gametes: in the following days it is possible to study the development of the released gametes. It is better to follow the growth of isolated gametes. In order to obtain quantitative data, we have studied isolated gametes, fixed with vapour, of a 2 per cent solution of osmium tetroxide for 5 min. and stained with Giemsa fluid, diluted 1 : 20 with distilled water.

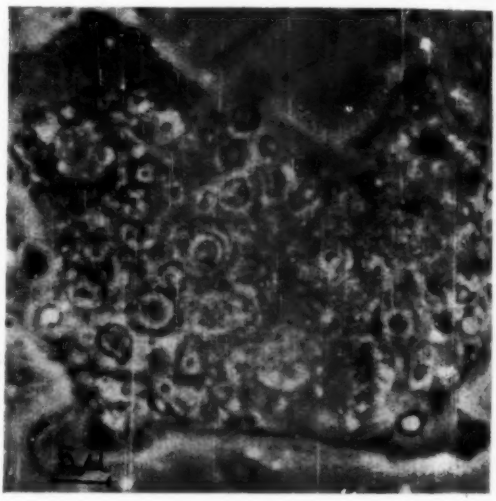

Fig. 2. Gametogenesis in *Amoeba spumosa*; the arrow shows a gamete that is escaping

The size of the gametes ranges between 2·6μ, which is the diameter of a gamete escaping from the mother amoeba, and 11μ: it takes about a fortnight for the gametes to reach this size. The gametes about five days old measure 6·8μ and at this time they copulate. The copulating gametes have the same size; therefore they appear to be isogametes and the zygote, as soon as it is formed, shows bilateral symmetry. A systematic study to see whether there are phenomena of relative sexuality is in progress.

Larger gametes, more than 7μ in diameter, correspond to a senescent stage. These large gametes, which did not copulate and will never copulate, undergo a slow degeneration. These large flagellate forms are, in fact, less stainable and show such a delicate protoplasmic structure that even a dilute staining solution may dissolve them.

The diagram (Fig. 3) illustrates the increase of four different gamete cultures at the stage before copulation. After the discovery of this increase we tried to study it from a cytological point of view. An increase in the size of the vacuoles, which are

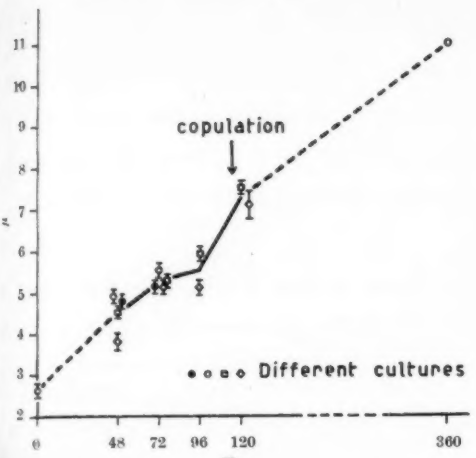

Fig. 3. Increase in diameter of the gametes of *Amoeba spumosa* after their release

placed at the gamete's anterior end, starts during the gamete growth. Some of these vacuoles contain small bodies intensely stained red by Giemsa fluid: they seem to be bacteria living in the culture medium. The conclusion, drawn from the study by the electron microscope[1], that a gamete ingests some bacteria and digests them in its vacuoles, is therefore confirmed. It seems, therefore, that gamete growth depends on true nutrition and not merely on an imbibition process by taking up water.

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VIROLOGY

Concentration of Poliovirus by an Aqueous Polymer Two-Phase System

With the technique for polio vaccine production used at present, the end-point titres often are in the neighbourhood of 10^6/ml., which is recommended as the lowest limit. Different methods have been tested to find a simple way for concentration of the virus. The physical and chemical methods proposed so far are rather complicated and give a comparatively low yield of virus[1]. Variations in the technique for cultivation of the virus have also been suggested as a means of increasing the virus titres[2].

In the experiments to be described here, a physico-chemical method for separation and concentration of macromolecules was used[3–5]. The method is based on the almost completely one-sided distribution of macromolecules which may be obtained when these are distributed in an aqueous two-phase system containing two different polymers. For concentration purposes, a phase system is constructed in such a way that the phase in which the virus particles are collected has a small volume compared with the original virus suspension. The virus is partially separated from other cellular constituents since these are distributed in a different manner[6,7,9].

In the present experiments, sodium dextran sulphate (prepared from a dextran fraction with a limiting viscosity number of 70 ml./gm.; sulphur content, 17 per cent; Pharmacia, Uppsala, Sweden) and polyethylene glycol ('Carbowax 6000'; Carbide and Carbon Chemicals Co., New York) were used for concentrations of poliovirus. Experiments with the same system have recently been made on *ECHO* virus[6]. The results of the application of the system to poliovirus, however, are considered worth while reporting, with regard to the possible use in vaccine production.

The polymers were added to harvested tissue culture fluid from *CHAT*-infected monkey kidney cultures until the final concentration was 0·2 per cent (w/w) dextran sulphate and 6·45 per cent polyethylene glycol. The virus suspension had previously been clarified by centrifugation for 10 min. at 2,000 r.p.m. In addition, a 5 *M* sodium chloride solution was added until the salinity of the total mixture was 0·3 *M*. After careful mixing, the system was allowed to separate for 24–48 hr. at + 4° C. Samples were then withdrawn from the top and the bottom phase and from the layer between these two—the interface. The titrations of the virus were carried out in monkey kidney tissue culture tubes, and logarithmic end-point titres were calculated.

A typical experiment gave the results shown in Table 1.

Table 1

	Virus titre/ 0·1 ml.	Volume (ml.)	Total amount of virus (*ID*50)
Original material	6·5	100	$3·2 \times 10^8$
Bottom phase (phase rich in dextran sulphate)	8·4	1·2	$3·0 \times 10^8$
Interface	7·7	—	—
Top phase (phase rich in polyethylene glycol)	4·6	134	$5·2 \times 10^7$

The bottom phase obtained represents about 1/100th of the total volume of the system. The virus, which accumulates in the bottom phase, is therefore concentrated 90–100 times. In controls, none of the polymers showed harmful effect on the virus. At the interface some proteins, probably cell debris, were precipitated. No change in the immunogenic capacity of the final preparation, measured in guinea pigs[10], was found.

The bottom phase contains 17 per cent dextran sulphate and is rather viscous; therefore it would be inconvenient as a vaccine preparation. The following methods were tested to remove the dextran sulphate:

(1) Precipitation by adding either 0·69 ml. 3 *M* potassium chloride or 0·3 ml. 1 *M* barium chloride per gm. bottom phase. All the virus activity remained in solution.

(2) Addition of 5 *M* sodium chloride to the collected bottom phase until the concentration of the sodium chloride became 1 *M*. By this procedure a new phase system was obtained. The volumes of the phases and the distribution of the virus in this system are shown by the results of the experiment recorded in Table 2.

In this secondary system almost all the dextran sulphate is in the bottom phase. Because of the changed molarity, more than 99 per cent of the virus is accumulated in the top phase. This contains only

Table 2

	Volume (ml.)	Titres/ 0·1 ml.	Amount of virus (*ID*50)
Original virus suspension	200	7·1	$2·6 \times 10^{10}$
Primary system : bottom phase	2·0	9·3	$4·0 \times 10^{10}$
Secondary system : top phase	0·5	9·8	$3·2 \times 10^{10}$
bottom phase	1·9	6·7	$9·5 \times 10^{7}$

dextran sulphate of the order of 0·1 per cent and in addition about 1 per cent polyethylene glycol. These small amounts of dextran sulphate may be eliminated by the chemicals suggested in (1). Since the volume of the top phase is about one-fifth of the total volume of the secondary system, a further concentration of virus is obtained.

The procedures described with poliovirus in the system dextran sulphate – polyethylene glycol leads to purification and a 100–500 times concentration of the virus. The product shows an antigenic capacity, which corresponds to the infectious titre measured by the cytopathogenic effect in tissue culture. Residual concentration of polymers in the concentrate is of the order of 0·1–1 per cent.

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SOIL SCIENCE

Diffusion of Ions in Soils

A knowledge of the speeds at which ions diffuse in soils is of both basic and agronomic importance, but the development of accurate methods for the measurement of diffusion coefficients has received little attention. During an investigation of the factors controlling the rate of diffusion, the following method has been evolved.

The value of the coefficient of diffusion (D) from Fick's law can be obtained for the system shown in Fig. 1, where at the time when the two sections of soil are placed in contact the amount of the ion under investigation is equal in the two halves, but in one a proportion consists of a radioactive isotope. The quantity of material Q which is diffused across the boundary CD in time t can be calculated from the relationship :

$$\frac{Q}{Q_\infty} = 1 - \frac{8}{\pi^2}\left[e^{-At} + \frac{e^{-9At}}{9} + \frac{e^{-25At}}{25} + \text{etc.}\right] \quad (1)$$

where $A = \frac{D\pi^2}{4L^2}$, L is the distance represented by AC and Q_∞ is the quantity which would cross the boundary in infinite time. When the value of $\frac{Q}{Q_\infty}$ is less than 0·5 this equation may be replaced by :

$$\frac{Q}{Q_\infty} = \frac{2}{L}\sqrt{\frac{Dt}{\pi}} \quad (2)$$

That either equation (1) or equation (2) may be employed according to the value of $\frac{Q}{Q_\infty}$ is illustrated by results for comparable experiments on the diffusion of rubidium (rubidium-86) in a Greensand soil. Using equation (1) for $\frac{Q}{Q_\infty} = 0·96$ a value of $6·19 \times 10^{-6}$ cm.^{2}/sec. was obtained for D, while the value from equation (2) when $\frac{Q}{Q_\infty} = 0·417$ was $6·13 \times 10^{-6}$.

By plotting graphically the theoretical relationship between $\frac{Q}{Q_\infty}$ and At of equation (1), a curve of the type shown in Fig. 2 is obtained. From this curve a value of A may readily be obtained given the experimental determination of $\frac{Q}{Q_\infty}$ for a known time t. D is then calculated from A. This simplified method has been found to give sufficient accuracy.

For experiments with soil, the conditions of the model shown in Fig. 1 are difficult to reproduce, since it is difficult to place two sections of soil in contact so that the boundary is sharp, and the subsequent separation and analysis are accurate. If the system is made so large that errors at the boundary are negligible, then experiments take an unduly long time to complete, for the root mean square displacement of the ions is proportional to $\sqrt{t}$. This problem of experimental procedure has been solved in the following way. It may be seen from Fig. 1 that

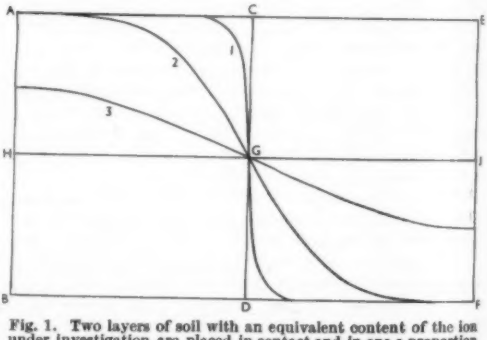

Fig. 1. Two layers of soil with an equivalent content of the ion under investigation are placed in contact and in one a proportion of the ions is present as the radioisotope. At the moment of contact the radioactive ions in section $ABDC$ are uniformly distributed and the height AB represents the value of the original concentration. As a result of the diffusion process radioactive material will move across the boundary CD into the section $CDFE$. As this process continues, the form of the distribution will change with time, as shown by the curves 1, 2 and 3. The line HGJ represents the final distribution after an infinite time

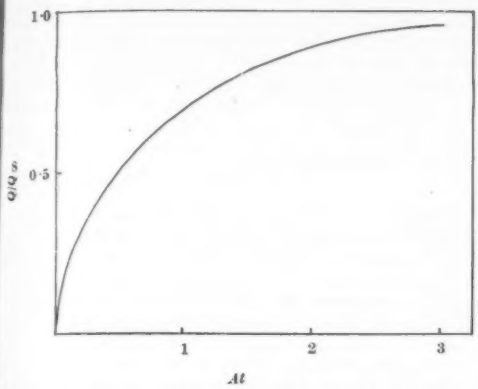

Fig. 2. The relationship of Q/Q_∞ and At as calculated from equation (1)

immediately the ions cross CD, the concentration at this boundary falls to a value represented by DG ($= \frac{1}{2}AB$) and afterwards remains at this level. If a thin sheet of a permeable ion-exchange material containing the diffusing ions at a concentration in equilibrium with DG is inserted between the two sections, the rate and pattern of movement in the soil will be affected to a negligible extent, provided first that the rate of diffusion in the exchange material is fast enough relative to that in the soil, and secondly, that the exchange capacity of the material is considerably higher than that of the soil. It has been found that 'Permaplex' ion-exchange membrane is suitable for this purpose. Calculations for the system indicate that the maximum error introduced by the resin is equivalent to less than 1 per cent of the length of the soil sections (AC of Fig. 1).

The method of experimentation is as follows. Two disks of the ion-exchange membrane are shaken individually in identical solutions containing equal aliquots of a given soil, but in one solution a radioactive isotope of the ion under investigation is incorporated. After equilibration with the soil the two disks are removed and held in contact for about 24 hr. until the radioactive ions have become uniformly distributed as a result of diffusion. One disk is then used to separate the equilibrated radioactive and inactive layers of the selected soil in a small closed cylinder the diameter of which is the same as that of the disk, that is, 1 in. The other disk may be kept to check that the disk in the cylinder does not gain or lose radioactivity during the experiment. The two layers of soil are later removed after a known time and extracted so that the quantities of radioactive material diffusing from one layer to the other may be measured. The value of the diffusion coefficients can then be calculated.

Diffusion coefficients vary with concentration, but the use of radioactive tracers makes it possible to measure differential coefficients of diffusion at exact concentrations under conditions where the total concentration is constant throughout the system but where a gradient of radioactive ions exists. Moreover, the tracer method also eliminates the complexities associated with the displacement of other adsorbed cations.

Using this technique it is possible to work with layers of soil only 2·5 mm. thick. The results so far obtained indicate that the diffusion coefficient may be as high as $1{\cdot}2 \times 10^{-7}$ cm.^{2}/sec. (corresponding to a root mean square displacement of 1·4 mm. in a day). Detailed experiments on one Greensand soil have so far shown that the rate of diffusion is considerably affected by compaction, being maximal at about 1·5 gm./ml. The effects of both temperature and the concentration of the soil solution suggest that a considerable part of the movement takes place when the cations are held in the exchange complex.

The research is now being extended to cover diffusion of several cations and anions in a variety of soils, together with a further analysis of the effects of the water content of the soil, the concentration of the soil solution, and temperature.

We wish to acknowledge our indebtedness to the Agricultural Research Council for a grant in support of this investigation.

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I. J. Graham-Bryce

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July 22.

Aluminium Ions in Aluminium Hydroxide, Phosphate and Soil–Water Systems

In recent years attention has been given to the solubility of aluminium phosphates in soils. Of the synthetic preparations examined, variscite, $Al(OH)_2H_2PO_4$, has been most extensively investigated and criteria for its existence in soils evaluated[1]. It has been assumed that the solubility product of variscite can be determined from the activities of the ionic species in the expression $K_{sp} = (Al^{3+})(OH^-)^3(H_2PO_4^-)$ and predictions of the phosphate content of soils have been made on this basis[2].

A recent investigation on the ionic species of aluminium in equilibrium with various forms of aluminium oxy-hydroxide and hydroxide has shown that for conditions usually found in soils, $AlOH^{2+}$, $Al(OH)_2^+$ or less-highly charged forms such as $Al_3(OH)_7^{2+}$ (strictly $[Al_3(OH)_7^{2+}]_n$, where n is an integer, but we assume the monomer, although the dimer is perhaps preferable) may be present in appreciable amounts. This means that these species may also determine K_{sp}.

For pH less acid than 4 in the presence of newly formed aluminium hydroxide (commonly called amorphous) and in an unbuffered system of very low ionic strength, the curve obtained on plotting the negative logarithm of the number of moles of aluminium per litre of solution [pAl_M] against the pH had a slope of 2, indicating that $[AlOH^{2+}][OH^-]^2$ = constant (curve C in Fig. 1). This curve agrees with the other workers' results for solubility and hydrolysis. In the presence of buffers, when the system was required to adapt itself to a demand for hydrogen ions by the buffer, more hydrolysis occurred and a curve (D) was obtained with a slope 2/3, which means that $[Al_3(OH)_7^{2+}][OH^-]^2$ = constant. When gibbsite was present, curve B resulted, which agrees with data in the literature on aged aluminium hydroxide. Experiments with diaspore showed that it was less soluble than the previous two forms and gave a curve (A) of slope 1 for pH less acid than 4·6, indicating that here $[Al(OH)_2^+][OH^-]$ = constant. Curve A also agreed with results from the literature for corundum and $Al(OH)_2^+$.

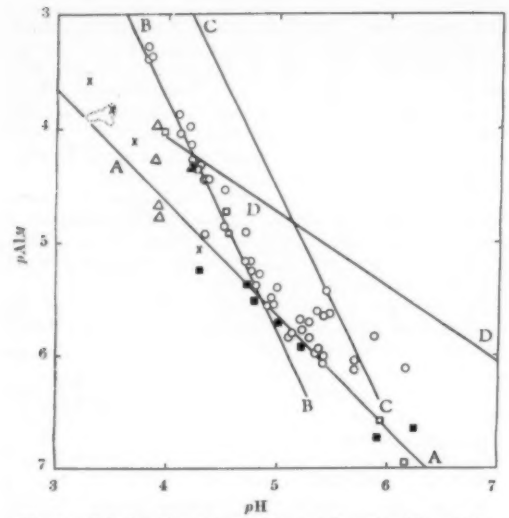

Fig. 1. Relationships between the negative logarithm of the number of moles of aluminium per litre of solution and the *p*H. Curve *A* as found for diaspore (■) and predicted for corundum dissolving as $Al(OH)_3^+$; curve *B* as found for gibbsite (□) and as predicted for aged aluminium hydroxide dissolving as $Al(OH)^{2+}$; curve *D* as found for fresh aluminium hydroxide in buffered systems (see text). Data for variscite (×), variscite–kaolinite (▲) and phosphated and unphosphated sodium and aluminium kaolinites (△) and for three soils (○) on treatment with 0·01 *M* calcium chloride are also given. The dotted points falling in a group on the upper left of the figure are for soils treated with 0·001 *M* hydrochloric acid and 0·01 *M* calcium chloride

It is of interest to superimpose on Fig. 1 results obtained by other workers for solutions in equilibrium with variscite, clays and soils.

The data for a variscite–kaolinite system[2] (represented by a single point in Fig. 1 where equilibrium has been reached after 56 days), for variscite[3] and for aluminium and sodium kaolinites phosphated and unphosphated[4], fall largely between lines *A* and *B*. The data for soils presented in Fig. 1 are for 0·01 *M* calcium chloride extracts of Hagerstown *s*.l., Greenville *f.s*.l. and Mardin *s*.l. (refs. 1, 5) (no activity corrections have been applied). The phosphate found in these solutions does not influence the position of the points in any uniform manner, although the range of variation of phosphate is greater than a hundredfold. This indicates that in these systems the important relationship is between pAl_M and *p*H (ref. 6). Not all soils would be expected to follow lines *A* and *B*. The data of earlier workers[7] on more acid soils lie for the greater part against line *C*, showing that $Al(OH)^{2+}$ was present and indicating that some Al^{3+} may be present under more acid conditions than *p*H 4·3. Again, the phosphate-level did not exert a systematic influence on the position of the points. These results show that the various aluminium hydroxides examined, amorphous, gibbsite and diaspore, may well represent stable phases in these soils. If variscite coexists as a discrete solid, its solubility does not appear to be fully exerted. On the other hand, it has long been advocated that the phosphate is bound to aluminium hydroxide to form a sorption compound.

The possible existence of variscite in some soils cannot, however, be discarded lightly, because soil–water systems have been observed to show reactions very similar to those of variscite, including the minimum phosphate solubility near *p*H 4 (ref. 8).

While the reactions giving rise to the solubility of variscite in more acid regions are reasonably clear, little is known of what occurs under more alkaline conditions. A possible reaction which would give rise to an increased solubility of variscite with increasing *p*H is:

$$H_2O + 3Al(OH)_2H_2PO_4 = Al_3(OH)_7^{2+} + 3H_2PO_4^- + H^+$$

This would give a slope of the *p*H and logarithm of the soluble phosphate curve which would be of the correct order for variscite and laboratory equilibria for a lateritic soil[8]. It would mean that the point of minimum solubility should be in the *p*H range 4·2–5·2 (that is, the intersection of curves *B* and *D* or *C* and *D*) as found in practice. If the kind of aluminium hydroxide present in a 'variscite' system is varied the value of the solubility product will vary so that care must be taken in extrapolating predictions from one situation to another even when it has been shown that the solubility of variscite is a controlling factor. It is clear that, for a detailed knowledge of reactions occurring in soil phosphate systems, it is necessary to study the ionic species present in the soil solution. The next step is to endeavour to determine which are the key reactions in the intricate interplay of processes taking place in the soil solution.

I hope to publish a full account of this work in due course.

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ARCHÆOLOGY

Recent Discoveries at Olduvai Gorge

As a result of the discovery in 1959 of the skull of *Zinjanthropus boisei*[1], in association with an Oldowan living floor at site *F.L.K.* I Olduvai, funds for a much more extensive programme at the end of 1959 and during 1960 were generously made available by the Wenner Gren Foundation, the Wilkie Foundation and the National Geographic Society of Washington, to all of which I express my deep gratitude.

After some preliminary work in December 1959 and January 1960, major excavations were started at site *F.L.K.* I (where the skull came from) in the middle of February 1960. These excavations are progressing very satisfactorily. An extensive and rich living floor of approximately 1–2 in. in thickness has been uncovered. It rests on a bentonitic deep-water clay and is immediately overlain by a consolidated deposit of water-laid volcanic sand. This living floor lies some 20 ft. below the uppermost deposit of Bed I.

Neither the underlying clay nor the overlying consolidated volcanic sand contains any large bones, nor any coarse material of any kind, and every large object lying on the living floor must have been brought there. All the larger animal bones have been broken open to obtain the marrow; all jaws and skulls of animals are smashed. A high proportion of the bones represent immature animals. Many more stone tools of the Oldowan culture have also been found.

Our hope of obtaining the mandible which belongs to the original *Zinjanthropus* skull has not, so far, been realized, but we now have a nearly complete tibia and fibula (Fig. 1), as well as what is probably a small piece of the pelvic girdle, together with some additional teeth and parts of the skull of a second individual, all from this original site.

The quantity of stone tools and flakes now available from this living floor will make it possible to assess the components of an industry of the Oldowan culture in great detail.

In addition to the excavations at this main site, a second site has been located, not far away, at what appears to be a slightly lower level of Bed I. This site is called *F.L.K.N.N.* I and, so far, it has yielded an amazing wealth of fossils—but only a very few artefacts.

The hominid fossils from this second site include fragments of a skull and some teeth, two clavicles (Fig. 2), a large part of a left foot (Fig. 3), six finger bones and two ribs. The animal fossils consist of a remarkable assemblage of genera and species, many of them new to Olduvai, and some unquestionably new to science.

Perhaps the most remarkable object from this second site (*F.L.K.N.N.* I) is a genuine bone tool (Fig. 4). This would appear to be some sort of a 'lissoir' for working leather. It postulates a more evolved way of life for the makers of the Oldowan culture than most of us would have expected.

Yet another site in Bed I (known as *F.L.K.N.* I) has been located during the past few weeks. This lies at a level some 20 ft. above the other two floors and immediately below the topmost deposit of Bed I. This third site consists of a very rich living floor with quantities of broken-up animal bones and many stone tools and flakes. Work on it has only just started.

Fig. 1. The tibia and fibula from site *F.L.K.* I

Fig. 2. One of the two clavicles from site *F.L.K.N.N.*

Fig. 3. Some of the bones of the left foot. The calcaneum is damaged

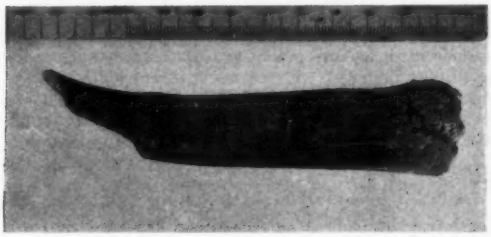

Fig. 4. Bone tool from site *F.L.K.N.N.* I

Excavations have also been conducted at a site known as *F.L.K.* II, which is stratigraphically well above the main *F.L.K.* I site, and this, as was expected, has yielded a fauna comparable to that of Olduvai sites *B.K.* II and *S.H.K.* II. The fauna is in direct association with an assemblage of artefacts of Stage 3 of the East African Chellean sequence.

The discovery of parts of hand and foot are of very special importance, for hitherto we have had no knowledge of these parts of the skeleton in early hominids.

This year's work has very strongly confirmed the statement which I made last year that Bed I is very distinct (both from the point of view of its fossil fauna and its culture) from Beds II, III, IV. Bed I is of Lower Pleistocene, or Villafranchian age; whereas Beds II, III and IV belong to the Middle Pleistocene.

As a result of the work carried out so far this year, the National Geographic Society has kindly made available a further grant to continue work for four or five more months.

L. S. B. Leakey

The Coryndon Museum,
Box 658, Nairobi,
Kenya.
Sept. 16.

[1] *Nature*, **184**, 491 (1959).

MISCELLANY

"Education of Scientists"

In his account of the British Association meeting on the education of scientists in *Nature*, October 22, p. 270, Prof. M. W. Thring reports that students who have obtained a General Certificate of Education examination in six subjects, of which three are at the Advanced Level, have reached the minimum requirements for entry to a university. These attainments are, in fact, much higher than are specified by the majority of British universities for entrance purposes.

In my own lecture, I was commenting on the high calibre of students joining the Diploma in Technology courses and expressing my satisfaction that, of the 700 students already accepted for these courses at the Northampton College of Advanced Technology, London, more than 300 had passed in three subjects at the Advanced Level in addition to the Ordinary Level requirements.

One other matter in the report needs clarification. In setting up the diploma in technology, the National Council for Technological Awards had clearly in mind that students who obtained first-class honours should be every bit as good as the first-class honours university graduate, and there is every reason to believe that these aims are being attained. The recommendation of the Committee of Vice-Chancellors and Principals to the Universities, that holders of the diploma in technology should be considered on the same footing as university graduates for registration for higher degrees, was an acceptance of this belief, and it is good to know that the recommendations have already been put into effect. In fact, one young man whose qualification is a diploma in technology has joined the academic staff of a provincial university.

James S. Tait

Northampton College of Advanced Technology,
St. John Street, London, E.C.1.

Cost of Scientific Periodical Publications

I refer to the figures showing the cost of scientific journals which have been given and discussed in recent issues of *Nature*. The figures quoted by Mr. K. W. Humphreys and Mr. H. D. Barry[1] give the comparable costs per page to libraries for various journals. (Incidentally, the cost of the *Biochemical Journal* is £4 per volume of approximately 620 pages, that is, 1·5*d*. per page, not 0·75*d*. as quoted.)

Captain Maxwell's table[2], however, compares the price charged to libraries for the *Journal of the Chemical Society* and some other journals with the price charged to individuals for the publications of Pergamon Press. Since fellowship of the Chemical Society is open to all approved persons throughout the world interested in the science, and one of the Society's main purposes is to disseminate chemical knowledge as widely and as cheaply as possible among scientists, it is proper to compare the price to Fellows with that of Pergamon journals to individuals. For the *Journal of the Chemical Society* the Fellows' price is approximately 0·5*d*. per page against a price to libraries of 1·0*d*. per page.

Captain Maxwell also states that a journal which has the backing of a scientific society has the advantage of a guaranteed circulation to its members, and, in most cases, a subsidy. These statements are incorrect if intended to apply to the Chemical Society, the only British publishing society mentioned in his table. The *Journal* is available only to those Fellows who choose to pay for it, and at the present time only some 16 per cent of Fellows exercise this option. Moreover, the Society does not receive any subsidy or outside grant for its publications, which are currently produced at a modest profit. I submit, however, that the prices quoted by your contributors show that this profit is not achieved by means of an unduly high price to libraries.

M. W. Perrin

The Chemical Society,
Burlington House, W.1.

[1] *Nature*, **186**, 124 (1960).
[2] *Nature*, **187**, 1052 (1960).

Capt. Maxwell's reply[1] to the paragraph concerning publication costs[2] is disingenuous; to show how cheap his publications are he compares his reduced price to private individuals with the top price of others to corporate subscribers. It is necessary in a fair comparison to compare 'like things with like'. Thus if, for example, *Tetrahedron* to the private individual costs 0·7*d*. per page, *Chemical Abstracts* to the private member subscriber costs 0·15*d*. per page, which brings our journal to the top of the list at a price and value which is second to none.

To say that journals backed by scientific societies have guaranteed circulation is unrealistic in most cases; it certainly is not true with *Chemical Abstracts*. Member subscribers to *Chemical Abstracts* are subsidized in an effort "to ensure maximum dissemination", but *Chemical Abstracts* has been on a self-supporting basis since 1956.

D. B. Baker

The Chemical Abstracts Service,
Ohio State University,
Columbus 10, Ohio.

[1] *Nature*, **187**, 1052 (1960).
[2] *Nature*, **186**, 124 (1960).

FORTHCOMING EVENTS

Monday, December 19

INSTITUTION OF MECHANICAL ENGINEERS, STEAM GROUP (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Discussion on "Safety on Construction Sites".

Tuesday, December 20

INSTITUTION OF ELECTRICAL ENGINEERS, MEASUREMENT AND CONTROL SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Discussion on "Digital Transducers", opened by Mr. L. Airey.

Wednesday, December 21

INSTITUTION OF ELECTRICAL ENGINEERS, ELECTRONICS AND COMMUNICATION SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. L. J. Ward: "Microminiaturization".

SOCIETY OF CHEMICAL INDUSTRY, CORROSION GROUP (at 14 Belgrave Square, London, S.W.1), at 6 p.m.—Discussion on "Practical Problems in Corrosion".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

ASSISTANT (graduate in mathematics, mathematical statistics or statistics, and preferably experience with punched cards and electronic computers) IN RESEARCH IN THE DEPARTMENT OF HUMAN ECOLOGY, to engage in the planning and the analysis of medical research projects—The Secretary of the Faculty Board of Medicine, The Medical School, The University, Tennis Court Road, Cambridge (December 31).

JUNIOR ASSISTANT LIBRARIAN (university graduate, preferably with some experience and/or professional qualifications in classification and cataloguing)—The Librarian, University College of North Staffordshire, Keele, Staffs (December 31).

LECTURER (with a degree in bacteriology or equivalent qualification) IN BACTERIOLOGY—The Secretary, West of Scotland Agricultural College, 6 Blythswood Square, Glasgow, C.2 (December 31).

POSTDOCTORAL RESEARCH FELLOW IN PHYSICAL CHEMISTRY, to study the properties of solids by mass spectrometry—The Registrar, The University, Edgbaston, Birmingham 15 (December 31).

SENIOR LECTURER IN ORGANIC CHEMISTRY; and a LECTURER IN ZOOLOGY, WITH SOME PHYSIOLOGY—The Registrar, Hatfield Technical College, Hatfield, Herts (December 31).

COMPUTATIONAL ASSISTANT (with a degree in mathematics or engineering or similar qualification, and preferably experience of the use of an electronic computer) IN THE DEPARTMENT OF MECHANICAL ENGINEERING, to use the university digital computer for work concerning the lubrication research which is going on within the Department—The Registrar, The University, Leeds 2 (January 6).

LECTURER (with qualifications in any of the branches of zoology, and preferably an interest in physiology, genetics or some other branch of experimental zoology) IN ZOOLOGY at the University of Tasmania, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, January 6).

SCIENTIFIC OFFICER or SENIOR SCIENTIFIC OFFICER (honours graduate in biochemistry and/or physiology, with appropriate research experience), to undertake research on hill sheep nutrition—The Secretary, Hill Farming Research Organization, 48 Palmerston Place, Edinburgh 12 (January 7).

CHADWICK CHAIR OF CIVIL ENGINEERING tenable at University College—The Academic Registrar, University of London, Senate House, London, W.C.1 (January 9).

FORESTERS (recently qualified university forestry graduates) in the New Zealand Forestry Service—The High Commissioner for New Zealand, 415 Strand, London, W.C.2, quoting Ref. B.11/9/8 (January 9).

HORTICULTURAL ADVISORY OFFICERS (with a degree in horticulture, preferably with practical experience in the production of horticultural crops, and in field advisory and experimental work) in the Agriculture Department, New Zealand, to advise growers on the production of horticultural crops, chiefly fruit and vegetables, undertake field experiments, and conduct surveys and special investigations—The High Commissioner for New Zealand, 415 Strand, London, W.C.2, quoting Ref. B.11/2/28 and Vacancy No. 3474 (January 9).

INSPECTORS OF EXPLOSIVES (2) (men or women at least 30 on November 1, 1960, with a degree (preferably first- or second-class) in chemistry or chemical technology, or equivalent qualification) with the Home Office, for duties involving travel to all parts of the country, and include advising on safety precautions for the manufacture, storage and conveyance of explosives; inspecting premises licensed for manufacture and storage; and advising on safety precautions for the storage and conveyance of petroleum and other dangerous substances—The Civil Service Commission, 17 North Audley Street, London, W.1, quoting S/5234/61 (January 10).

CHAIR OF CIVIL ENGINEERING—The Registrar, University College, Singleton Park, Swansea (January 14).

FISHERY INVESTIGATING OFFICERS (male, physically fit, with an honours degree in zoology, and prepared to spend considerable time in the field) in the Marine Department, New Zealand, to undertake local investigations and advise on biological aspects of freshwater fisheries management and development problems in all parts of New Zealand, with headquarters in Wellington—The High Commissioner for New Zealand, 415 Strand, London, W.C.2, quoting Ref. B.11/15/6 and Vacancy No. 3271 (January 16).

SOIL SURVEYORS (2) (graduates in botany, chemistry, geography, geology or agriculture and preferably with previous experience in soil survey, particularly in the tropics) in the Regional Research Centre for the West Indies, Faculty of Agriculture, University College of the West Indies, Trinidad—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (January 20).

LECTURER (part time), to investigate respiratory functions in childhood—The Secretary, Institute of Child Health (University of London), Great Ormond Street, London, W.C.1 (January 21).

ASSOCIATE PROFESSOR OF MEDICAL BIOCHEMISTRY IN THE DEPARTMENTS OF MEDICINE AND BIOCHEMISTRY, University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, January 23).

CHAIR OF PARASITOLOGY in the University of Malaya, Singapore—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (January 31).

LECTURER or ASSISTANT LECTURER IN ELECTRICAL ENGINEERING—The Registrar, The University, Southampton (January 31).

SENIOR LECTURER IN CIVIL ENGINEERING (STRUCTURES) at the University of Western Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, January 31).

EXPERIMENTAL OFFICERS (preferably with a pass degree or H.N.C., and a knowledge of electrical and electronic methods of measuring displacement, velocity, acceleration, strain and temperature under vibration conditions and experience in the design of electronic circuitry would be an advantage) to set up and operate instrumentation for an interesting programme of environmental testing. Duties will include the design of special electronic instruments to meet particular requirements—The Senior Recruitment Officer, U.K.A.E.A., A.W.R.E., Aldermaston, Berks, quoting Ref. A.2684/34.

HEAD (man or woman, with a good honours degree and experience) OF THE MATHEMATICS DEPARTMENT—The Headmistress, Queen Anne's School, Caversham, Reading.

NATIONAL RESEARCH COUNCIL AND OTHER POSTDOCTORAL FELLOWSHIPS IN THE DEPARTMENT OF PHYSICS—Prof. H. E. Duckworth, Chairman, Department of Physics, McMaster University, Hamilton, Ontario, Canada.

PHYSIOLOGIST or ZOOLOGIST (with a good degree in physiology or zoology, preferably with Ph.D., and interests and experience in the field of mammalian reproduction) in a small unit investigating the biochemical and physiological properties of cervical secretions, with particular reference to fertility—The Secretary, National Institute for Research in Dairying (University of Reading), Shinfield, Reading, Berks, quoting Ref. 60/17.

READER (able to show evidence of research ability in the academic and industrial fields, and preferably with experience in the food industry) IN FOOD PROCESSING AND FOOD ENGINEERING—The Principal, National College of Food Technology, St. George's Avenue, Weybridge, Surrey.

RESEARCH ASSISTANT (preferably with an honours degree in physical and inorganic chemistry) IN THE DEPARTMENT OF MINERALOGY AND PETROLOGY, for a programme of research concerning fundamental solid-state problems in the field of cement chemistry—Dr. J. D. C. McConnell, Department of Mineralogy and Petrology, Downing Place, Cambridge.

RESEARCH ENGINEER (with an honours degree in chemical engineering and proved research ability) IN THE DEPARTMENT OF CHEMICAL ENGINEERING, to work under Prof. Edgeworth Johnstone on the dimensional scaling-up of a particular type of process plant—The Registrar, The University, Nottingham.

SENIOR TECHNICIAN II (with special experience in bacteriology) to take charge of a laboratory—The Secretary, Forest Group Hospital Management Committee, Langthorne Road, Leytonstone, London, E.11.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Ciba (A.R.L.), Limited. Technical Notes No. 212 (August, 1960): The "Bluebird" C.N.7. Pp. 8. (Duxford: Ciba (A.R.L.), Limited, 1960.) [149

British Welding Research Association. Fifteenth Annual Report, 1959–60. Pp. 64. (London: British Welding Research Association, 1960.) [149

Hopkin and Williams, Ltd. Organic Chemical Reagents. Monograph No. 40: 2:9-Dimethyl-1:10-Phenanthroline ("Neocuproine"): Reagent for Copper. By E. J. Newman and G. Peters. Pp. 6. (Chadwell Heath, Essex: Hopkin and Williams, Ltd., 1960.) [149

Henry Wiggin and Co., Ltd. Incoloy DS: Heat-Resisting Nickel-Chromium-Iron Alloy. Pp. 7. (London: Henry Wiggin and Co., Ltd., 1960.) [149

A Bibliography of Farm Buildings Research, 1945–1958. Part 3: Buildings for Poultry. Pp. 84. (London: Agricultural Research Council, 1960.) 4s. 6d. [149

Television and the Family. (A Report on an Enquiry designed and directed by Dr. W. A. Belson, and carried out by the Audience Research Department of the B.B.C. under the supervision of Professors A. R. Knight, M. G. Kendall, P. E. Vernon, and Barbara Wootton.) Pp. xx+151. (London: British Broadcasting Corporation, 1959.) [149

New Check List of British Agarics and Boleti. By R. W. G. Dennis, P. D. Orton, and F. B. Hora. (Supplement to *Transactions of the British Mycological Society*, June 1960.) Pp. 225. (London: Cambridge University Press, 1960.) 15s. net; 2.50 dollars. [149

Department of Scientific and Industrial Research, and Fire Offices' Committee Joint Fire Research Organization. Fire Research 1959: Report of the Fire Research Board with the Report of the Director of Fire Research. Pp. viii+63+8 plates. (London: H.M. Stationery Office, 1960.) 5s. [149

Science Masters' Association. Provision and Maintenance of Laboratories in Grammar Schools (1959). (Results of a Questionnaire issued in 1959 by the Science Masters' Association, Association of

Women Science Teachers, National Union of Teachers, and Joint Four Secondary Association.) Pp. 16. (London: John Murray, 1960. Published for the Science Masters' Association.) 1s. net. [149

National Union of Teachers. Treasure Chest for Teachers: Services available to Teachers and Schools from Societies and Associations which have some bearing on various aspects of the School Curriculum. Pp. 94. 3s. Mathematics in the Primary School. By R. A. Swallow. (Curriculum Studies, No. 1.) Pp. ii+44. 2s. 6d. Science in the Primary School. By Cedric Griggs. (Curriculum Studies, No. 2.) Pp. 35. 2s. (London: The Schoolmaster Publishing Co., Ltd., 1960.) [149

Department of Scientific and Industrial Research: Building Research Station. Factory Building Studies, No. 7: Structural Frameworks for Single-Storey Factory Buildings. By H. V. Apcar. Pp. v+34. (London: H.M. Stationery Office, 1960.) 4s. net. [149

Price's (Bromborough) Limited. Technical Publication No. 7: Water Conservation—Bibliography of References in the Published Literature including some of the chief references to the literature in Allied Fields. Pp. 70. (Bromborough Pool, New Ferry, near Birkenhead: Price's (Bromborough), Ltd., 1960.) [149

Annual Report on the Meteorological Office for the year April 1, 1959 to March 31, 1960. Pp. 55+4 plates. (M.O. 683.) (London: H.M. Stationery Office, 1960.) 4s. net. [149

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The National Foundation for Educational Research in England and Wales, in association with the Institute of Education, London University. Occasional Publication No. 2: Spelling Irregularity and Reading Difficulty in English. By Dr. W. R. Lee. Pp. i+74. (London: National Foundation for Educational Research in England and Wales, 1960.) 10s. [149

Philosophical Transactions of the Royal Society of London. Series A: Mathematical and Physical Sciences. No. 1022, Vol. 253 (8 September 1960): Laminar Boundary-Layer Flow Near Separation with and without Suction. By R. M. Terrill. Pp. 55–100. 14s. 6d. No. 1023, Vol. 253 (8 September 1960): On a Differential Equation of Boundary-Layer Theory. By W. A. Coppel. Pp. 101–136. 11s. (London: Royal Society, 1960.) [149

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A Short History of the Battle of Britain to commemorate the 20th Anniversary. By John P. Milford Reid. Pp. 26. (London: Air Ministry, 1960.) [149

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Cymdeithas Diogelu Harddwych Cymru. Council for the Preservation of Rural Wales. Annual Report, 1958–1959. Pp. 77+5 plates. (London: Council for the Preservation of Rural Wales, 1960.) [219

The Relation of Dietary Fats to Chronic Degenerative Diseases. By Dr. H. M. Sinclair. (A lecture given at Apothecaries Hall on 4th March, 1960.) Pp. ii+24. (London: Brown and Polson, Ltd., 1960.) [219

Current Medical Research: a reprint of the articles in the Report of the Medical Research Council for the year 1958–1959. Pp. v+56. (London: H.M. Stationery Office, 1960.) 3s. 6d. net. [219

Acheson Colloids Limited, Plymouth. A List of "Gredag" Greases and Special Compounds. Pp. 12. (Plymouth: Acheson Colloids, Ltd., 1960.) [219

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Proceedings of the Nutrition Society of Southern Africa, Vol. 1. Pp. xiii+104. (Pretoria: Nutrition Society of Southern Africa, 1960.) [149

United States Department of Commerce: Coast and Geodetic Survey. Publication 65–1, Part 11: Plane Coordinate Intersection Tables (2½ minute)—Illinois. Pp. iii+124. (Washington, D.C.: Government Printing Office, 1960.) 60 cents. [149

Commonwealth Scientific and Industrial Research Organization, Australia. Outline of Activities at May 1, 1960. Pp. 11. Divisions and Sections at May 1, 1960. Pp. 19. (Melbourne: Commonwealth Scientific and Industrial Research Organization, 1960.) [149

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A Collection of Papers of the Rational Theory. By F. Harrison Stamper. Pp. 13. (Los Angeles, Calif.: F. Harrison Stamper, 1990 Barnett Road, 1960.) [149

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Food and Agriculture Organization of the United Nations. Animal Health Yearbook, 1959. Pp. ii+249. (Rome: Food and Agriculture Organization of the United Nations; London: H.M. Stationery Office, 1960.) 12s. 6d.; 2.50 dollars. [149

Deutscher Wetterdienst. Mittlere Niederschlagssummen (mm) für die Bundesrepublik Deutschland: Jahr und Hydrologische Halbjahre. Zeitraum: 1891–1930. Bearbeiter: Hans Schirmer. Pp. 3+2 maps. (Offenbach a. M.: Selbstverlag des Deutschen Wetterdienstes, 1960.) [149

United States Department of the Interior: Geological Survey. Bulletin 1071-G: Geomorphology of the Upper Kuskokwim Region, Alaska. By Arthur T. Fernald. Pp. v+191–279+plates 21 and 22. Bulletin 1082-E: Strategic Graphite: a Survey. By Eugene N. Cameron and Paul L. Weis. Pp. v+201–321+plates 8–11. 1.25 dollars. Bulletin 1083-D: Pulse-Transient behavior of Brine-Saturated Sandstones. By George V. Keller. Pp. iii+111–129. 15 cents. Bulletin 1084-G: Method for the Quantitative Spectrochemical Analysis of Rocks, Minerals, Ores, and other Materials. By Harry Bastron, Paul R. Barnett, and K. J. Murata. Pp. iii+165–182. 15 cents. Bulletin 1085-B: Botanical Prospecting for Uranium in the Deer Flat Area, White Canyon District, San Juan County, Utah. By Albert J. Froelich and Frank J. Kleinhampl. Pp. iii+51–84+plate 6. 65 cents. Bulletin 1112-B: Chemical Composition as a Guide to the Size of Sandstone-Type Uranium Deposits on the Morrison Formation on the Colorado Plateau. By A. T. Miesch, E. M. Shoemaker, W. L. Newman and W. I. Finch. Pp. iv+17–61. 25 cents. (Washington, D.C.: Government Printing Office, 1960.) [149

United States Department of the Interior: Geological Survey. Water-Supply Paper 1453: Quality of Surface Waters of the United States, 1956. Parts 9–14: Colorado River Basin to Pacific Slope Basins on Oregon and Lower Columbia River Basin. Prepared under the direction of S. K. Love. Pp. xiii+447. Water-Supply Paper 1454: Methods for Collection and Analysis of Water Samples. By F. H. Rainwater and L. L. Thatcher. Pp. ix+301. 1.50 dollars. Water-Supply Paper 1459-F: A Survey of Pertinent Biochemical Literature. By Eugene T. Oborn. Pp. iv+111–190. Water-Supply Paper 1488: The Geology and Ground-Water Resources of Calcasieu Parish, Louisiana. By Alfred H. Harder. Pp. vi+102+plates 1–9. Water-Supply Paper 1489: Geology and Ground Water in the Platte-Republican Rivers Watershed and the Little Blue River Basin above Angus, Nebraska. By C. R. Johnson. With a section on Chemical Quality of the Groundwater by Robert Brennan. Pp. iv+142+plates 1–4. 1.25 dollars. (Washington, D.C.: Government Printing Office, 1960.) [149

United States Department of the Interior: Geological Survey. Water-Supply Paper 1540-A: Residue Method for Common Minor Elements. By Joseph Hafftу. Pp. iii+9. 15 cents. Water-Supply Paper 1541-A: General Introduction and Hydrologic Definitions. By W. B. Langbein and Kathleen T. Iseri. (Manual of Hydrology: Part 1. General Surface-Water Techniques.) Pp. iii+29. 20 cents. Water-Supply Paper 1541-C: Graphical Correlation of Gaging-Station Records. By James K. Searcy. (Manual of Hydrology: Part 1. General Surface-Water Techniques.) Pp. iv+67–100+plate 1. (Washington, D.C.: Government Printing Office, 1960.) [149

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Fisheries Research Board of Canada. Bulletin No. 122: Measuring the Production of Marine Phytoplankton. By J. D. H. Strickland. Pp. viii+172. 2 dollars. Bulletin No. 123: Further Midwater Trawl Developments in British Columbia. By W. E. Barraclough and W. W. Johnson. Pp. v+45. 50 cents. (Ottawa: Queen's Printer, 1960.) [219

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